*Curriculum Vitae*Peng Chen

PERSONAL DATA

Born	June 27, 1979.	Address：	College of Chemistry,
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EDUCATION

2003-2007	Ph.D in Chemistry, The University of Chicago	Chicago, USA
2002-2003	M.S. in Chemistry, The University of Chicago	Chicago, USA
1998-2002	B.S. in Chemistry, Peking University	Beijing, China
1999-2002	B.S. Double degree in Economics, Peking	Beijing, China

POSITIONS

2015/01-	Chairman, Department of Chemical Biology, Peking University, Beijing, China
2014/08-	Professor with Tenure, Department of Chemical Biology,
2011/05-	Investigator, Peking-Tsinghua Center for Life Sciences,
2009/07 -2014/07	Investigator, Department of Chemical Biology, College of Chemistry, Peking University, Beijing
2007-2009	Postdoctoral Fellow, The Scripps Research Institute, San Diego. *Advisor: Prof. Peter G. Schultz*
2002-2007	Research Assistant, The University of Chicago, Chicago. *Advisor: Prof. Chuan He*

RESESARCH INTERESTS

- Protein bioorthogonal chemistry
- Intracellular protein labeling and manipulation
- Host-pathogen interactions
- Protein therapeutic engineering

AWARDS

2015	China Association for Instrumental Analysis (CAIA) Award
2015	The Chemical Society of Japan Distinguished Lectureship Award
2015	Young Science and Technology Innovation Talents (China)
2014	Roche Chinese Young Investigator Award
2014	(RSC) Chem Soc Rev Emerging Investigator Lectureship
2014	CAPA Biomatik Distinguished Faculty Award
2013	National Young Scientists Award (China)
2013	National Program for Special Support of Eminent Professionals (China)
2012	National Natural Science Funds for Distinguished Young Scholar (China)
2012	CCS (Chinese Chemical Society) Young Investigator Award
2012	SCOPUS Young Scholar, Elsevier.
2011	WuXi PharmaTech Life Science and Chemistry Award.
2011	Instructor award for the “Challenge Cup” undergraduate research competition at PKU.

2007 Elizabeth R. Norton Prize for excellence in research in chemistry, The University of Chicago.
2005 Society of Cosmetic Chemists Award.
2004 Burroughs Wellcome Fellowship, Burroughs Wellcome Fund.

PUBLICATIONS

As an independent PI.

55 Li J, **Chen P*** " Bioorthogonal chemistry beyond ligation: bond-cleavage reactions, applications and outlook", ***Nat. Chem. Biol.*** Accepted.

54 Song Y, Yang M, Wegner S, Zhao J, Zhu R, Wu Y, He C*, **Chen P*.** "A genetically encoded FRET sensor for intracellular Heme", ***ACS Chem. Biol***. (2015), 10,1610-5.

53 Wang J, Cheng B, Chen X*, **Chen P*.** "Chemically Remodeling of Cell-Surface Sialic Acids by Using the Palladium-Triggered Bioorthogonal Elimination Reactions", ***Angew. Chem. Int. Ed.*** (2015),*54*, 5364-8.

52 Hackenberger C*, **Chen P***. "Synthetic biomolecules: Synthetic protein modifications-a giant leap towards understanding and generating biological functions". ***Curr. Opin. Chem. Biol.*** , (2015), doi: 10.1016/j.cbpa.2015.09.005.

51 Lin R, Elf S, Shan C, Kang HB, Ji Q, Zhou L, Hitosugi T, Zhang L, Zhang S, Seo JH, Xie J, Tucker M, Gu TL, Sudderth J, Jiang L, Mitsche M, DeBerardinis RJ, Wu S, Li Y, Mao H, **Chen P**, Wang D, Chen GZ, Hurwitz SJ, Lonial S, Arellano ML, Khoury HJ, Khuri FR, Lee BH, Lei Q, Brat DJ, Ye K, Boggon TJ, He C, Kang S, Fan J, Chen J*. "6-Phosphogluconate dehydrogenase links oxidative PPP, lipogenesis and tumour growth by inhibiting LKB1-AMPK signaling". ***Nat Cell Biol***. (2015), *11*, 484-96.

50 Zhang G, Zheng S,**Chen P***. "Illuminating biological processes through site-specific protein labeling", ***Chem. Soc. Rev.*** (2015), *44,* 3405-17. (Invitation for *Emerging Investigator Lectureship Award 2014*).

49 Yang M,**Chen P***, "Progress in the bioorthogonal labeling reactions", ***Acta. Chim. Sinica***, (2015), *73*, 783-92.

48 Li J, Jia S, **Chen P*** "Diels-Alder reaction-triggered bioorthogonal protein activation in living cells", ***Nat. Chem. Biol.,*** (2014), *10*, 1003-5.
[This work has been highlighted by *Nature Methods,* 2015, *12*,16]

47 Yang M, Jolloh A, Wei W, Zhao J*, Wu P*, **Chen P***, "Biocompatible click chemistry enabled compartment-specific pH measurement inside *E. coli*", ***Nat. Commun***. (2014), *5*, 4981.
[This work has been highlighted by ***Chem. & Eng. News.*** 2014, *92(39),* 30]

46 Lin S, He D, Long T, Zhang S, Meng R, **Chen P***, "Genetically Encoded Cleavable Protein Photocrosslinker", ***J. Am. Chem. Soc.*** (2014), *136*, 11860-3.
[This work has been highlighted by *Chem. & Eng. News.* 2014, *92(34),* 4]

45 Lin S, **Chen P*.** "Virus engineering: Fighting HIV at its own game." ***Nat. Chem***. (2014), *6*. 566-8.

44 Zheng S, Zhang G, Li J, **Chen P***. "Monitoring Endocytic Trafficking of Anthrax Lethal Factor via Precise and Quantitative Protein Labeling". ***Angew. Chem. Int. Ed.,*** (2014), *53*, 6449-53.

43 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.
[This work has been highlighted by ***Nature Chemical Biology,***2014,*10*,328***, Nature Methods,***

2014,*11*,472]

42 Yang M, Li J, **Chen P***."Transition Metal Mediated Biocompatible Protein Chemistry in Living Cells". ***Chem. Soc. Rev.*** (2014), 43, 6511-26. *Emerging Investigators Special Issue.*

41 Hao Z, Lou H, Zhu R, Zhu J, Zhang D, Zhao B, Zeng S, Chen X, Chan J, He C*, **Chen P***. "The multiple antibiotic resistance regulator MarR is a copper sensor in *Escherichia coli*" ***Nat. Chem. Biol.*** (2014), 10, 21-8.
[This work has been highlighted by ***(RSC) Chemistry World***]

40 Yang Y, Lin S, Lin W, **Chen P***."Ligand-assisted Dual-site Click Labeling of EGFR on Living Cells" ***ChemBioChem***. (2014), *15*, 1738-43.

39 Ming Cheng, Wei Zhang, Jinghe Yuan, Wangxi Luo, Nan Li, Shixian Lin, Yi Yang, Xiaohong Fang*, **Chen P***."Single-molecule dynamics of site-specific labeled transforming growth factor type II receptors on living cells", ***Chem. Comm***. (2014) ,50, 14724-7

38 Shan C, Elf S, Ji Q, Kang HB, Zhou L, Hitosugi T, Jin L, Lin R, Zhang L, Seo JH, Xie J, Tucker M, Gu TL, Sudderth J, Jiang L, DeBerardinis RJ, Wu S, Li Y, Mao H, **Chen P**, Wang D, Chen GZ, Lonial S, Arellano ML, Khoury HJ, Khuri FR, Lee BH, Brat DJ, Ye K, Boggon TJ, He C, Kang S, Fan J, Chen J*. "Lysine Acetylation Activates 6-Phosphogluconate Dehydrogenase to Promote Tumor Growth.", ***Mol. Cell.*** (2014), 55, 552-65.

37 Fan Y, Zhao J, Yan Q, **Chen P*** and Zhao D*. "A Water-soluble Triscyclometalated Organoiridium Complex: Phosphorescent Nanoparticle Formation, Nonlinear Optics, and Application for Cell Imaging". ***ACS Appl. Mat. Inter.*** (2014) ,*6*, 3122-31.

36 Ge X, Wang R, Ma J, Liu Y, Ezemaduka AN, Chen P, Fu X*, and Chang Z*. "DegP primarily functions as a protease for the biogenesis of β-barrel outer membrane proteins in the Gram-negative bacterium Escherichia coli". ***FEBS J.*** (2014), 281, 1226-40.

35 Li J, Lin S, Wang J, Jia S, Yang M, Zhang X, Hao Z, **Chen P*** "Ligand-free Palladium-mediated Site-specific Protein Labeling inside Gram-negative Bacterial Pathogens". ***J. Am. Chem. Soc***. (2013) *135*, 7330-8.

34 Zhao J, Lin S, Huang Y, Zhao J*, **Chen P***. Mechanism-Based Design of a Photoactivatable Firefly Luciferase". ***J. Am. Chem. Soc***. (2013), *135*, 7410-3.

33. Lin S, Yan H, Li L, Yang M, Peng B, Chen S, Li W* and **Chen P***, "Site-specific Engineering of Chemical Functionalities on the Surface of Live Hepatitis D Virus" ***Angew. Chem. Int. Ed***., (2013), 52, 13970-4.

32 Chang H, Han M, Huang W, Wei G, Chen J, **Chen P**, Chen R, Zhang J, Xu T*, Xu P*. "Light-induced protein translocation by genetically encoded unnatural amino acid in Caenorhabditis elegans". ***Protein Cell***. (2013),*4*, 883-6

31 Zhao B, Zhang G, Zeng S, He C, and **Chen P***. "Probing subcellular organic hydroperoxide formation via a genetically encoded ratiometric and reversible fluorescent indicator.", ***Integr. Biol*** (2013), 5,1485-9.

30 Liu J, Karpus J, Wegner S, **Chen P***, He C*. "Genetically Encoded Copper(I) Reporters with Improved Responses for Use in Imaging", ***J. Am. Chem. Soc.*** **(**2013), *135:*3144-9.

29 Yang M, Song, Y, Zhang M, Lin S, Hao Z, Liang Y, Zhang D, **Chen P*.**
"Converting a solvatochromic fluorophore into a protein-based pH indicator for extreme acidity"

Angew. Chem. Int. Ed., (2012) *51*, 7674-9.

28 Li Y, Yang M, Huang Y, Song X, Liu L,* **Chen P*.** "Genetically encoded alkenyl-pyrrolysine analogues for thiol-ene reaction mediated site-specific protein labeling", ***Chem. Sci.***, (2012), 3, 2766-70.

27. Li J, **Chen P*.** "Moving Pd-mediated Protein Cross-coupling to Living Systems" ***ChemBioChem.*** (2012), 13, 1728-31.

26. Wang J, Karpus J, Zhao B, Luo Z, **Chen P,** He C*. "A selective fluorescent probe for carbon monoxide imaging in living cells." ***Angew. Chem. Int. Ed.,*** **(**2012), 51, 9652-6.

25. Li Y, Yang M, Huang Y, **Chen, P*,** Liu L*. "Ligation of Expressed Protein α-Hydrazides via Genetic Incorporation of an α-Hydroxy Acid." ***ACS Chem. Biol.*** (2012), *7*, 1015-22.

24. Wei W, Zhu T, Wang Y, Yang H, Hao Z, **Chen P*,** Zhao J*. *"Engineering a gold-specific regulon for cell-basedvisual detection and recovery of gold."* ***Chem. Sci.*** (2012), *3***,** 1780-4.

23. Liu J, Zhang M, **Chen P***. "Probing pH Mediated protein-protein interactions via photocrosslinking", ***SCIENTIA SINICA Chimica.*** (2012) *42*, 1694-9.

22. Li J, Wang J, **Chen P*.** "Unnatural amino acid mediated Protein Bioorthogonal Labeling" ***ACTA CHIMICA SINICA*** (2012),*70*, 1439-45.

21. Chen X, Hao Z, **Chen P*.** "Protein photocrosslinking reveals dimer of dimers formation on MarR protein in *Escherichia coli*" ***SCIENCE CHINA Chemistry*** (2012). *42*, 223-5.

20 Zhang M, Lin S, Song X, Liu J, Fu Y, Fu X, Chang Z*, **Chen, P*.** "A genetically incorporated crosslinker reveals chaperone cooperation in acid resistance", ***Nat. Chem. Biol***, (2011), *7*, 671-7. [This work is a "News Coverage" on ***Chem. & Eng. News.*** *Sep 7, 2011*， and has been highlighted by ***Nature Asia-Pacific*** on *Sep 5, 2011*]

19 Lin S, Zhang Z, Xu H, Li L, Chen S, Li J, Hao Z, **Chen P*.** "Site-specific incorporation of photocrosslinker and bioorthogonal amino acids into enteric bacterial pathogens*", **J. Am. Chem. Soc.*** (2011), *133*, 20581-7.

18. Hao Z, Song Y, Lin S, Yang M, Liang Y, Wang J, **Chen P*.** "A readily synthesized cyclic pyrrolysine analogue for site-specific protein 'click' labeling". ***Chem Commun (Camb)*** (2011). *47*, 4502-4.

17. Hao Z., Hong S., Chen X*, **Chen, P*.** "Introducing Bioorthogonal Functionalities into Proteins in Living Cells", ***Acc. Chem. Res.,*** (2011), *44*, 742-51.

16. **Chen P*,** Brugarolas P, He C*. "Redox Signaling in Human Pathogens",***Antioxid Redox. Signal.,*** (2011), *14(6)*, 1107-18.

15. Zhao B, Liang Y, Song Y, Zheng C, Hao Z, **Chen P*.** "A Highly Selective Fluorescent Probe for Visualization of Organic Hydroperoxides in Living Cells". ***J. Am. Chem. Soc***. (2010). *132*, 17065-7.

14. Zhao J, **Chen P*.** "Discovery of mystery in Ribosome-introduction of the 2009 Nobel Prize in Chemistry." ***University Chemistry***, (2009), *24*, 1-5.

<u>From Ph.D and Postdoc Research</u>

13. **Chen P,** Dan G, Guo J, Ou W, Geierstanger B, Schultz PG. "A facile system for encoding unnatural amino acids in mammalian cells", ***Angew Chem. Int. Ed***. (2009), *48*, 4052-5.

12. Ai H, Shen W, Sagi A, **Chen P.** Schultz PG "Probing protein-protein interactions with a genetically encoded photo-crosslinking amino acid." ***ChemBioChem***. (2011), *12*, 1854-7.

11. Dan G, **Chen P,** Peters F, Schultz PG. "A genetically encoded epsilon-N-methyl lysine in mammalian cells", ***ChemBioChem,*** (2010), *11*, 1066-8.

10. **Chen P,** Nishida S, Poor C, Cheng, A, Bae T, Kuechenmeister L, Dunman P, Missiakas D, He C. "A new oxidative sensing and regulation pathway mediated by the MgrA homologue SarZ in *Staphylococcus aureus*" ***Mol. Microbiol***. (2009), *71*, 198-211.

9. Poor C, **Chen P,** Duguid E, Rice P, He C. "Crystal structures of the reduced, sulfenic acid, and mixed disulfide forms of SarZ, a redox active global regulator in *Staphylococcus aureus*". ***J. Biol. Chem.*** (2009), 284(35), 23517-24.

8. **Chen P,** He C. "Selective recognition of metal ions by metalloregulatory proteins", ***Curr. Opin. Chem. Biol.*** (2008), *12(2)*, 214-21**.**

7. Chen H, Hu J, **Chen P,** Lan L, Li Z, Hicks L, Dinner A, He C. "The *Pseudomonas aeruginosa* multidrug efflux regulator MexR uses an oxidation sensing mechanism", ***Proc. Natl. Acad. Sci. USA***. (2008), *105* (36), 13586-91.

6. **Chen P,** Wasinger E, Zhao J, van der Lelie D, Chen L, He C. "Spectroscopic insights into lead(II) coordination by the selective lead(II)-binding protein PbrR691" ***J. Am. Chem. Soc.*** (2007), *129*, 12350-1.

5. Sarkar S, Andoy N, Benitez J, **Chen P,** Kong J, He C, Chen P. "Engineered holliday junctions as single-molecule reporters for protein-DNA interactions with application to a MerR-family regulator" ***J. Am. Chem. Soc.*** (2007)**,** *129*, 12461-7.

4. Wegner S, Okesli A, **Chen P,** He C "Design of an emission ratiometric biosensor from MerR family proteins: A sensitive and selective sensor for Hg^{2+}", ***J. Am. Chem. Soc*.** (2007), *129*, 3474-5.

3. **Chen P,** Bae T, Williams W, Duguid E, Rice P, Schneewind O, He C. "An oxidation sensing mechanism is used by a global regulator MgrA in *Staphylococcus aureus*", ***Nature Chem. Biol.*** (2006), *2*, 591-5.
[A Science and Technology Concentrate highlighting this work appears in ***Chem. & Eng. News*** *84* [41] 31 (2006). The finding described in this paper had also been registered in the *Infectious Disease Biomarker Database* as a potential biomarker for *Staphylococcus aureus* vancomycin resistance.]

2. **Chen P,** Greenberg B, Taghavi S, Romano C, van der Lelie D, He C. "An exceptionally selective lead(II)-regulatory protein from *Ralstonia metallidurans*: development of a fluorescent lead(II) probe", ***Angew Chem. Int. Ed.,*** (2005), *44*, 2715-9.
[This work had been highlighted by ***Chem. & Eng. News*** *83* [15] 26 (2005); *Brookhaven National Laboratory News, April 4, 2005; and several German based newspapers.*]

1. **Chen P,** He C. "Constructing highly sensitive and selective fluorescent biosensors for metal ions by using the MerR family proteins", ***J. Am. Chem. Soc.*** (2004), *126*, 728-9.

Books

1. Jiang H, Chen Y, **Chen P,** Zhang L, "Chemical Biology Frontier and Perspective". ***China Science Publishing*** (2013), ISBN: 978-7-03-037949-8

2. Liu L, **Chen P,** Zhao J, He C. "Principles of Chemical Biology", ***China Science Publishing Group***, ISBN: 978-7-03-028767-0.

3. "The development Strategy of Chemical Biology in China", ***China Science Publishing Group***, (2015), ISBN: 978-7-03-043399-2.

4. "China Medical Technology Report", ***China Science Publishing Group***, (2015), Chapter 3. ISBN:

978-7-03-043439-5.

Patents

(1) **US Patent** "A Facile System for Encoding Unnatural Amino Acids in Mammalian Cells" **Chen P,** Groff D, Guo J, Bernhard G, Schultz PG. (2010), Publication #: **WO2010/114615**

(2) **US Patent** "Identifying a modulator of bacterial MgrA function by contacting the MgrA polypeptide or its fragment with a candidate substance and assessing the binding of the MgrA polypeptide to a target DNA" **Chen P**, He C. (2007), Publication #: **WO2007/090123**

TEACHING

- *Fall 2013-present*, "Chemical Biology Track", Graduate Course, CLS, PKU
- *Fall 2009-present*, "Introduction to Chemical Biology", Graduate Course, PKU.
- *Spring 2012-present*, "Bioinorganic Chemsitry", Graduate Course, PKU
- *Fall 2010-2014*, "Today's Chemistry", Freshman Course, PKU.
- *2013-present*, Chair of the Curriculum Design Committee, CLS, PKU.
- *2011-2015*, Member of the Teaching Committee, College of Chemistry, PKU.

MAJOR GRANTS

- NSFC Innovation Research Group (#21521003), "Chemical Biology Study of Cell fate regulation", *National Science Foundation of China (NSFC)*, 2016-2021.
- NSFC Major Project (#21432002), "Chemical modification and regulation of biomolecules in plants", *National Science Foundation of China (NSFC)*, 2015-2019.
- NSFC Major Research Project, Phase II (#91313301), "Chemical Biology probes for studying signaling transduction pathways", *National Science Foundation of China (NSFC)*, 2014-2015
- NSFC Distinguished Young Scholar (#21225206), "Chemical Biology", *National Science Foundation of China (NSFC)*, 2013-2016.
- National 973 Project (#2012CB917300), "Biogenesis, modification, assembly and quality control of membrane proteins". *Ministry of Science and Technology (MOST*), 2012-2016.
- National 973 Project (#2010CB912300), "Genetic-code expansion technique for Protein Labeling", *Ministry of Science and Technology (MOST*), 2010-2014.
- NSFC Major Project (#20932006), "New Organic reactions and approaches for living cell chemistry", 2010-2013.
- NSFC Incubation Project (#91013005), "New Protein photocrosslinker to study the signal transduction mechanism of bacteria biofilm formation, *National Science Foundation of China* 2011-2013.
- NSFC Young Scientist Project (#21001010), " Development and mechanistic study of biosensors for selective metal recognition", *National Science Foundation of China* ,2011-2013.
- High Education Research Project, "Mechanistic study of bacterial acid-resistance", *Ministry of Education (MOE*), 2011-2012.
- International Collaboration Project, *Pfizer Inc, USA.* "Evolution of Super Sortase for improved ligation efficiency". 2011-2013.

Summary of Achievements

Dr. Peng Chen, Professor of Chemical Biology, Peking University

[Summary] Dr. Peng Chen's laboratory is interested in exploiting biocompatible exogenous chemistry to dissect intracellular protein activities (eg. interactions, signaling transductions and dynamic localizations). Using these newly developed intracellular protein-chemistry tools, his lab investigates the molecular mechanisms underlying host-pathogen interactions.

Bioorthogonal chemical reactions have become a powerful tool for selective modification of biomolecules in living systems. However, these reactions have largely centered on in situ labeling of biomolecules topologically located on the surface of mammalian or bacterial cells. Protected by single or double plasma membranes, **biomolecules located in the highly fragile and active internal spaces of prokaryotic and eukaryotic cells represent attractive yet challenging targets for bioorthogonal labeling**.

Dr. Peng Chen started his independent career as an Investigator at Peking University in 2009. **His lab has been focused on developing biocompatible strategies to label and manipulate proteins within the intracellular space of living cells, particularly with those proteins involved in host-pathogen interactions**. Infectious disease is a major threaten to human health worldwide and is a more serious issue in developing countries. The causative pathogens employ a wide array of protein effectors to subvert host defense and establish infection. His lab has been developing intracellular protein-chemistry toolkit to investigate these essential proteins during host-pathogen interactions. He has made some technological innovations or novel findings in this cutting edge direction. Overall, he has clearly established himself as a leader among young scientists working at the Chemistry-Biology Interface in China, and also gained international reputation for some of his research achievements, which will be summarized below:

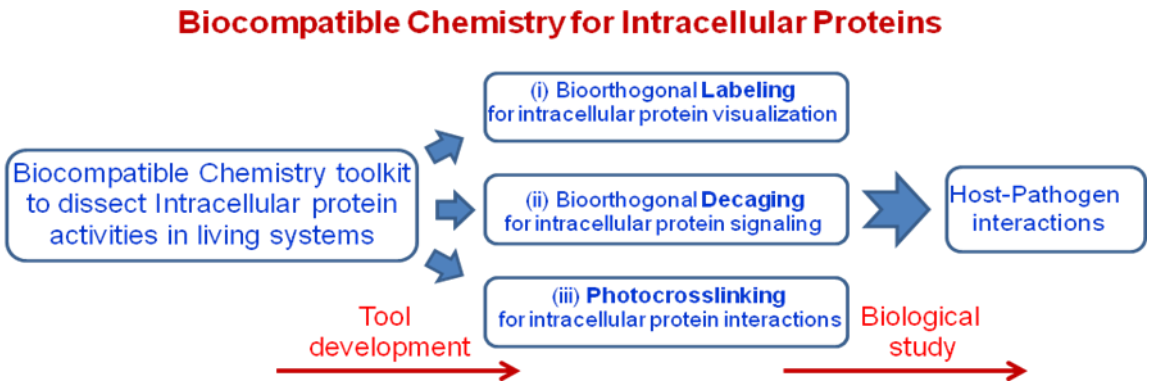

Fig. 1 Bioorthogonal chemistry toolkit in dissecting intracellular protein activities.

1. Bioorthogonal Reactions for Intracellular Protein Labeling

***Tool development*:**

1.1 **Intracellular Click-labeling**. New ligand-assisted copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reactions for labeling proteins within internal spaces of *E. coli* cells: (i) periplamsic protein labeling (***Angew. Chem. Int. Ed.,*** 2012, *51*, 7674), (ii) cytoplasmic protein labeling (***Nat. Commun***., 2014, *5*, 4981).

1.2 **Pd-mediated Intracellular Cross-coupling**. Palladium-catalyzed Sonogashira cross-coupling reactions for intracellular protein labeling and visualization in Gram-negative bacterial cells (***J. Am. Chem. Soc***., 2013, *135*, 7330).

Biological study:

1.3 **Toxin and Virus Visualization**. Using these bioorthogonal labeling tools to (i) monitor endocytic trafficking of Anthrax lethal factor in host cells (***Angew. Chem. Int. Ed.,*** 2014, *53*, 6449), (ii) label Hepatitis virus HBV and HDV (***Angew. Chem. Int. Ed.,*** 2013, 52, 13970), as well as (iii) visualize toxin effectors inside enteric pathogens *Shigella* and *Salmonella* (***J. Am. Chem. Soc.,*** 2011, *133*, 20581).

1.4 **pH-gradient across Bacterial Membrane**. *In situ*-labeled, protein-based pH sensors inside *E. coli* cells allowed the compartment-specific pH measurement in bacterila periplasmic vs. cytoplasmic spaces. The PMF (proton motive force) values across *E. coli* cytoplasmic membrane under normal and stress conditions were calculated, which is an essential factor in supporting bacterial antibiotic resistance and acid-resistance (***Nat. Commun.,*** 2014, *5*, 4981).

2. Bioorthogonal "Elimination" Reactions for Intracellular Protein Decaging and Activation

***Tool development*:**

2.1 **Pd-mediated Chemical Decaging**. Palladium-catalyzed deprotection reactions as a biocompatible chemical decaging strategy to rescue protein activity in living cells (***Nat. Chem.*** 2014, *6*, 352)

2.2 **iD-A reaction Mediated Bioorthogonal Decaging**. *inverse-electron-demand* Diels–Alder reaction (iD-A) was converted to a highly effieicnt and bioorthogonal decaging method for intracellular protein activation (***Nat. Chem. Biol.,* 2014,** *10*, 1003).

The above two bioorthogonal elimination reactions have also been expanded to (i) additional types of biomolecules such as Glycans in living cells (***Angew. Chem. Int. Ed.,*** *under revision)*, and (ii) inside living animals (*manuscript in preparation***).**

Biological study:

2.3 **Chemically-controlled Toxin Activation inside Host Cells**. Chemical decaging-controlled activation of a conserved *Shigella* TypeIII secretion effector OspF (phosphor-lyase) inside living mammalian host cells, which revealed the damaging effects of this toxin on host MAPK (Mitogen-activated protein kinases) pathways ***(Nat. Chem.,*** 2014, *6*, 352)

The Bioorthogonal Elimination reactions exhibited high efficiency and low toxicity for chemical decaging of proteins which is complementary to the protein photo-decaging reactions developed previously (***J. Am. Chem. Soc.,*** 2011***,*** *135*, 7410). In certain applications, particularly within live animals, small-molecule mediated chemical decaging can be advantageous. Currently, his lab is applying the lysine "decaging" method to protein kinases, which all contain a highly conserved lysine residue within the catalytic domain as the ATP acceptor. By using this bioorthogonal decaging strategy, they blocked specific kinase's activity in living cells, which allowed the subsequent gain-of-function study of each kinase within the intracellular signaling transduction network.

3. Photocrosslinking Reactions for Profiling Intracellular Protein-Protein Interactions

***Tool development*:**

3.1 **Genetically-encoded Protein Photocrosslinker**. A diazirine-containing photocrosslinking unnatural amino acid for highly efficient and non-invasive identification of transient protein-protein interactions inside living cells. (***Nat. Chem. Biol.,*** 2011, *7*, 671).

3.2 **Cleavable Photocrosslinker**. A second-generation, selenium-based cleavable photocrosslinking amino acid was recently developed, which allows the seperation of bait and prey proteins after crosslinking, thus enhanced the capturation and seperation efficiency for proteomic analysis (***J. Am. Chem. Soc.,*** 2014, *136*, 11860).

Biological study:

3.3 **Bacterial acid-resistance mechanism**. The genetically encoded photocrosslinker allowed the profiling of client proteins of a major acid chaperone-HdeA within the cellular envelop of enteric bacterial pathogens including EPEC and *Shigella*. This work revealed a unique chaperone coorperation network that is essential for supporting acid resistance of these pathogens that have to survive through the highly acidic human stomach to establish infections in human intestine (***Nat. Chem. Biol,*** 2011, *7*, 671).

3.4 **Bacterial antibiotic-resistance mechanism.** A novel antibiotic-triggered copper signaling pathway was discovered that potentiates bacterial antibiotic tolerance through a major antibiotic resistance regulator-MarR in *E. coli*. The photocrosslinker permitted the identification of copper(II)-triggered dimer-of-dimer formation of MarR inside bacterial cells (***Nat. Chem. Biol.,*** 2014, *10*, 21).

Overviews of these aforementioned intracellular protein manipulation tools developed by Chen group have been summarized by two invited review articles ***(Acc. Chem. Res***. 2011, *44*, 742. and ***Chem. Soc. Rev***. 2014, *43*,6511.).

[Awards and Grants] Peng Chen has been well recognized with many awards, including: RSC Chem Soc Rev Emerging Investigator Lectureship (2014), Chinese-American Professors Association Biomatik Distinguished Faculty Award (2014), Roche Chinese Young Investigator Award (2014), China Young Scientists Award (2013), Chinese Chemical Society Young Investigator Award (2012), Distinguished Young Scholar by Natural Science Funds of China (2012), and WuXi PharmaTech Life Science and Chemistry Award (2011). His lab is supported by multiple grants from National Natural Science Funds of China (NSFC), Ministry of Science and Technology (MOST), and Ministry of Education (MOE).

[Promoting Chemical Biology Community in China] Peng Chen has been dedicated to promote the Chemical biology research in China. He has organized multiple national meeting on Chemical Biology and is also the organizer of the National Chemical Biology Young scientists Association. He is the co-authors of a Chemical biology textbook (in Chinese), as well as two Chemical Biology Frontier Books (one published by the China Academy of Sciences and the other published by Natural Science Funds of China).