



# Xiaoguang Lei

Prof. Xiaoguang Lei obtained BS degree in chemistry at Peking University in 2001. He then conducted his PhD research in natural product synthesis and chemical biology from 2001 to 2006 with Prof. John. A. Porco, Jr. at Boston University. After two years (2006-2008) as a post-doctoral fellow in Prof. Samuel J. Danishefsky's group at Columbia University, he started the independent research at National Institute of Biological Sciences (NIBS) in China as a PI. In early 2014, he joined the faculty of college of chemistry at Peking University.

Prof. Lei's major research interests are chemical biology, natural product synthesis and medicinal chemistry. In the chemical biology field, he has systematically utilized various small molecule probes including complex natural products to dissect the TNF- $\alpha$  initiated extrinsic programmed cell death pathways including both apoptosis and programmed necrosis (necroptosis), and illuminate a number of new molecular mechanisms underlying these fundamental cellular processes. These endeavors have been highlighted by several seminal discoveries: (1) using small molecule probe NSA to identify the mixed lineage kinase domain-like protein (MLKL) as a novel interacting protein with RIP3 and elucidate an unprecedented molecular mechanism of necroptosis (Cell 2012); (2) using a chemical biology approach to develop the first selective small molecule activator of the death receptor 5 (DR5) to efficiently trigger apoptosis of cancer cells (Nature Chemical Biology 2013); (3) using natural product kongnesin A to uncover a new mechanism for blocking necroptosis through the selective inhibition of protein-protein interaction between heat shock protein 90 (Hsp90) and its co-chaperon CDC 37 (Cell Chemical Biology 2016). In addition, he also focuses on function-oriented synthesis and has accomplished a number of remarkable total syntheses of structurally complex and bioactive natural products (ACIE 2012, 491; JACS 2012, 12414; Chem. Sci. 2013, 1163; ACIE 2014, 9257; Nature Commun. 2014, 4614; ACIE 2015, 1011; JACS 2015, 11946; ACIE 2016, 3112). Moreover, he has been further exploring, and with significant success aspects of target identification and mode of action for these complex natural products (Nature Communications 2015; ACIE 2014, 12111; ACIE 2016, 4291).

Prof. Lei has received several academic awards including the prestigious 2017 Tetrahedron Young Investigator Award in Bioorganic and Medicinal Chemistry, and Young Chemical Biologist Award by the International Chemical Biology Society 2013.

#### Key publications:

1. Sun, L.; Wang, H.; Wang, Z.; He, S.; Chen, S.; Liao, D.; Wang, L.; Yan, J.; Liu, W.; Lei, X.\*; Wang, X.\* "Mixed Lineage Kinase Domain-like Protein Mediates Necrosis Signaling Downstream of RIP3 Kinase" Cell 2012, 148, 213-227
2. Wang, G.\*; Wang, X.; Yu, H.; Wei, S.; Williams, N.; Holmes, D. L.; Halfmann, R.; Naidoo, J.; Wang, L.; Li, L.; Chen, S.; Harran, P.; Lei, X.\*; Wang, X.\* "Small Molecule Activation of the TRAIL Receptor DR5 in Human Cancer Cells" Nat. Chem. Biol. 2013, 9, 84-89.
3. Dong, T.; Li, C.; Wang, X.; Dian, L.; Zhang, X.; Chen, X.; Li, L.; Cao, R.; Huang, N.; He, S. \*; Lei, X.\* "Ainsliadimer A selectively inhibits IKK $\alpha/\beta$  by covalently binding a conserved cysteine" Nat. Commun. 2015, 6, 6522.