Title: A chemo-enzymatic approach for preparation of branched and head-to-tail semisynthetic cyclic peptide using split-intein; and traceless in vivo ubiquitylation in mammalian cells

Cyclic peptides are important class of biomolecules finding diverse application in basic research and drug discovery. Due to their superior physicochemical properties as compared to their linear counterparts, they are considered as ideal candidates for studying protein-protein interactions. Key to success of cyclic peptides as potential therapeutics has been screening large chemical space of canonical and noncanonical amino acid residues. Therefore, over the years several methods have been reported to generate diverse library of cyclic peptides. However, most of the methods developed in recent years to prepare cyclic peptides focus either on a synthetic or a recombinant route. While the former provides access to diversified, noncanonical peptides, including unnatural and D-amino acid, for example, the latter can harness the power of genetic randomization to generate and select from large peptide libraries. I will discuss a chemo-enzymatic method to make semisynthetic cyclic peptides in vitro combining advantage of both synthetic and genetically encoded fragments using protein trans-splicing and bioorthogonal oxime ligation. I will also discuss sortase A catalysed site-specific in vivo ubiquitylation of proteins in mammalian cells and its application to engineer various cellular processes.