

Ph. D. Open Seminar

Department of Chemistry, IISER Bhopal

Title of thesis: “Single-site labeling of Lysine in native proteins through multicomponent approach”

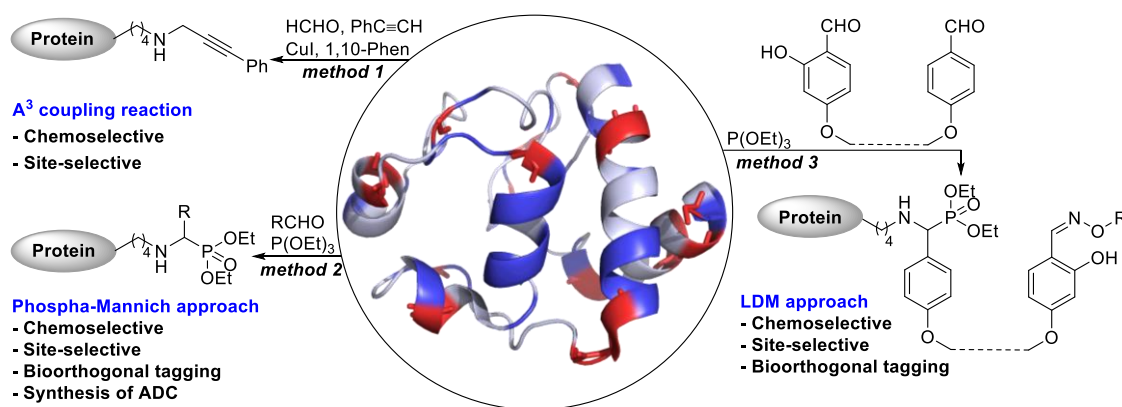
Speaker: Maheshwerreddy Chilamari (Thesis advisor: Dr. Vishal Rai) **Roll No:** 1210208

Date: 15/02/2018

Time: 05:00 pm

Venue: AB-II 401

Attachment of tags to the proteins provides utility platforms for biologics, biomaterials, and biophysics.¹ A chemical technology that can deliver single-site labeling of endogenous proteins would be ideal to meet these requirements. The challenge in the identification of a site with unique reactivity emerges from the abundance of functional groups with similar reactivity. It is complicated further by the presence of multiple copies of each residue.² We have developed multicomponent approaches that offer single-site installation of propargyl (method 1)^{3,4} and aminophosphonate (method 2)^{4,5} groups to ϵ -amine of native proteins in physiological conditions. In both the methodologies, the selective labeling of most reactive ϵ -amine is achieved in a pool of nucleophilic residues, α -amine, and several copies of ϵ -amine. These results validate that a chemical transformation can differentiate subtle differences in the reactivity of protein backbone residues. Finally, we developed a modular linchpin directed methodology (method 3)⁶ for the modification of ϵ -amine beyond the most reactive lysine residue.⁶ The methods deliver orthogonal tagging of protein with probes and synthesis of antibody-drug conjugates for directed cancer chemotherapeutics.



¹ Krall, N.; da Cruz, F. P.; Boutureira, O.; Bernardes, G. J. L. *Nat. Chem.* **2016**, *8*, 103-113.

² Landa, P.; Adusumalli, S. R.; Chilamari, M.; Rai, V. *Chem. Commun.* **2017**, *53*, 959-962.

³ Chilamari, M.; Landa, P.; Rai, V. *Chem. Eur. J.* **2017**, *23*, 3819-3823.

⁴ Rai, V.; Chilamari, M.; Purushottam, L. Patent application 201621030484, Sept 7, 2016; PCT/IN2017/050362, August 31, **2017**.

⁵ Chilamari, M.; Kalra, N.; Shukla, S.; Rai, V. *Manuscript under preparation*.

⁶ Chilamari, M.; Sahu, T.; Adusumalli, S. R.; Kalra, N.; Shukla, S.; Rai, V. *Manuscript under preparation*.