

Ph.D. Open Seminar

Department of Chemistry, IISER Bhopal

Title of Thesis: "Catalysis by proteins and their site-selective bioconjugation"

Speaker: Pralhad Namdev Joshi (Thesis advisor: Dr. Vishal Rai)

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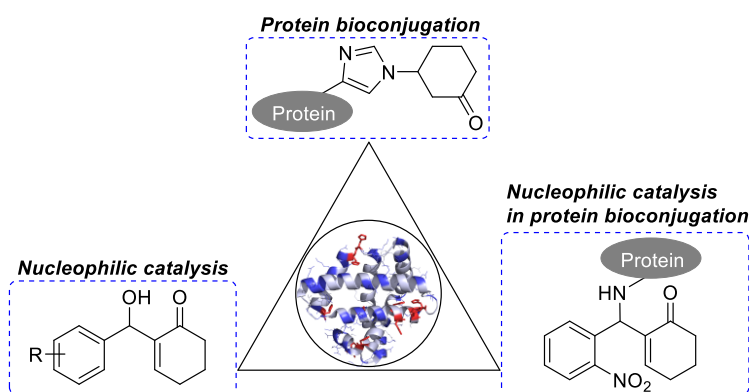
Date: 24th December 2018 (Monday)

Time: 4:00 PM

Venue: AB2-401

The nucleophilic residues in enzymes are instrumental in regulating their activity. These electron rich functionalities have also been found to catalyze chemical transformations beyond their natural role in the biological systems.¹ In this perspective, we have developed a methodology where the promiscuous nature of a protein has been capitalized to render efficient nucleophilic catalysis. Here, His and Arg pair forms a catalophore in the low-order protein assembly.²

The nucleophilic residues also serve as targets in the modification of proteins. The precise bioconjugation provides the platform for biophysical investigations, cell imaging, and development of biologics.³ Here, the glimpse of immense opportunities came with pre-engineered proteins where unnatural amino acids or peptide-based recognition motifs delivered bio-orthogonal site-specific labeling.⁴ Our group is involved in the development of chemical technologies for precision labeling of native proteins. At first, we developed a protocol for single-site phthalimidation of α -amine at the N-terminus of peptides and proteins.⁵ Next, we developed a minimalistic electrophile for single-site labeling of His residue. Interestingly, a chemically triggered reversibility protocol allowed us to extend the methodology for metal-free purification of proteins with His-tag.⁶ Finally, we demonstrated that a protein could serve as both catalyst and substrate in a multi-component reaction. The generation of complementary intermediates on two different molecules exploits protein-protein interaction for single-site labeling.⁷



¹ O'Brien, P. J.; Herschlag, D. *Chem. Biol.* **1999**, *6*, 91.

² Joshi, P. N.; Purushottam, L.; Das, N. K.; Mukherjee, S.; Rai, V. *RSC Advances* **2016**, *6*, 208.

³ Krall, N.; da Cruz, F. P.; Boutureira, O.; Bernardes, G. J. L. *Nat. Chem.* **2016**, *8*, 103.

⁴ Spicer, C. D.; Davis, B. G. *Nat. Commun.* **2014**, *5*, 4740.

⁵ Singudas, R.; Adusumalli, S. R.; Joshi, P. N.; Rai, V. *Chem. Commun.* **2015**, *51*, 473.

⁶ Joshi, P. N.; Rai, V. *Manuscript under revision*.

⁷ Joshi, P. N.; Reddy, N. C.; Rai, V. *Manuscript under preparation*.