Ph.D. Open seminar

Department of Chemistry, IISER Bhopal

Title of Thesis: "Precision in modification and analysis of proteins by targeting amine and carboxylic acid"

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Nature inspire chemists to develop tools for precise labeling of proteins to engineer their properties.[1] It demands a chemical strategy to render selectivity under mild conditions. However, the large pool of nucleophiles and their multiple copies offered by the protein surface make the task highly challenging. In this regard, we have developed a phthalimidation protocol that addresses the above challenges and delivers single-site modification of N-terminus α-amine.[2] The tunable reactivity of the amphoteric intermediate under mild reaction conditions is the key to success. Subsequently, we developed a method for single-site modification of carboxylic acid. Contrary to amine, it is a daunting task to achieve even chemoselectivity in this case. We developed a strategy that re-defines the reactivity landscape of protein to enable the single-site labeling of carboxylic acid.[3] Here, the functional group participates in a multi-component reaction sequence where both intramolecular and intermolecular irreversible pathways can deliver the desired product. This chemical platform allows the single-site installation of the ^{19}F-NMR probe and a fluorophore.

The lack of unambiguous characterization tools for protein bioconjugates has been one of the bottlenecks in the field. To address this, we developed the analytical sensitivity booster that enhances the peptide detection up to attomolar concentration in mass spectrometry (MS).[4] In turn, it allows a remarkable improvement in peptide mapping. Also, it delivers simplified and enhanced detection of peptide fragments in the MS-MS. Overall, it provides a tool for thorough analysis of proteins, antibodies, and their bioconjugates.

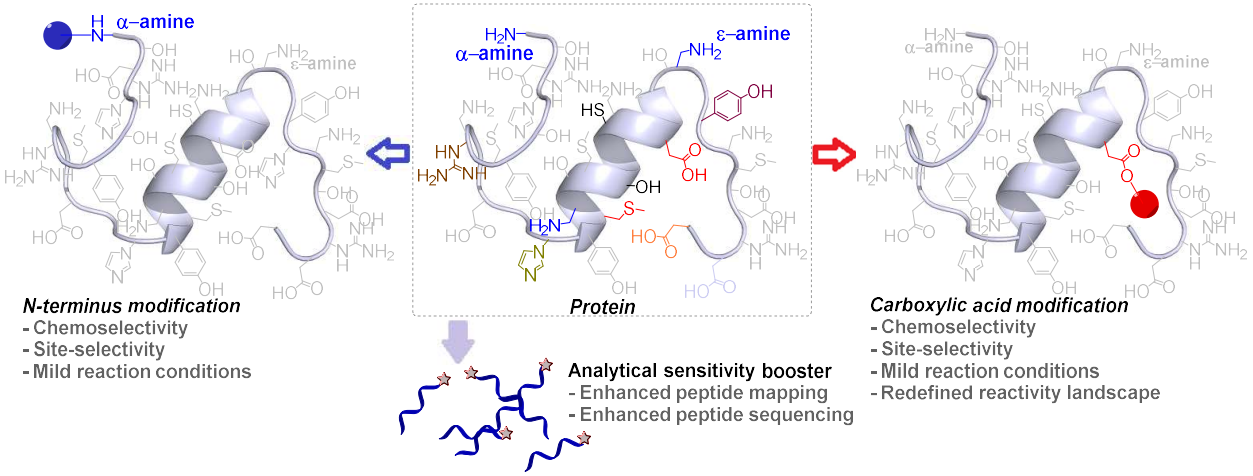

Figure. Reactivity, selectivity, and analysis of proteins.

[1] Krall, N.; da Cruz, F. P.; Boutureira, O.; Bernardes, G. J. L. *Nat. Chem*. **2016**, *8*, 103-113.
[2] Singudas, R.; Adusumalli, S. R.; Joshi, P. N.; Rai, V. *Chem. Commun.* **2015**, *51,* 473-476.
[3] Singudas, R.; Rai, V. *Manuscript under preparation.*
[4] Singudas, R.; Sahu, T.; Rai, V. *Manuscript under preparation.*