

LDM® platform (Patent granted)

The first-ever platform establishes simultaneous regulation of reactivity, chemoselectivity, site-selectivity, site-modularity, and residue modularity. Besides meeting the technological demands of biochemistry and biophysics, this comprehensive technology for precision engineering of proteins renders homogeneous antibody-drug conjugates (ADCs) for directed cancer chemotherapeutics and antibody-fluorophore conjugates (AFCs) for image-guided surgery. Currently, our team is working towards the translation of selected candidates towards pre-clinical investigations. Also, the recent developments demonstrate that the platform enables protein and organelle specificity within the cells and living organisms.

[1] Linchpin empowers promiscuous electrophile to render site-selective modification of histidine and aspartic acid in proteins, Rawale, D. G.; Thakur, K.; Pranav, S.; Sajeev, T. K.; Ramesh, A.; Adusumalli, S. R.; Mishra, R. K.; **Rai, V.** *Chem. Sci.* **2021**, *12*, 6732-6736. Impact factor: 9.346

[2] Chemoselective and site-selective lysine-directed lysine modification enables single-site labeling of native proteins, Adusumalli, S. R.; Rawale, D. G.; Thakur, K.; Purushottam, L.; Reddy, N. C.; Kalra, N.; Shukla, S.; **Rai, V.** *Angew. Chem. Int. Ed.* **2020**, *59*, 10332-10336. Impact factor: 15.34

[3] Single-site labeling of native proteins enabled by a chemoselective and site-selective chemical technology, Adusumalli, S. R.; Rawale, D. G.; Singh, U.; Tripathi, P.; Paul, R.; Kalra, N.; Mishra, R. K.; Shukla, S.; **Rai, V.** *J. Am. Chem. Soc.* **2018**, *140*, 15114-15123. Impact factor: 15.42

Gly-tag® technology (Patent filed)

It provides the first-ever chemical technology for N-Gly specific modification. Recently, a segment of biologists has been developing engineered enzymes to meet the related technological demands. However, our already established Gly-tag technology provides a remarkable advantage in specificity, efficiency, and cost factors. With this breakthrough, our group is investigating the immense possibilities in the field of cell-surface engineering and precision therapeutics.

[4] Single amino acid Gly-tag enables metal free protein purification, Purushottam, L.; Unnikrishnan, V. B.; Rawale, D. G.; Gujrati, M.; Mishra, S. D.; Sajeev, T. K.; Reddy, N. C.; Adusumalli, S. R.; Mishra, R. K.; **Rai, V.** *Chem. Sci.* **2020**, *11*, 13137-13142. Impact factor: 9.346

[5] Single-site glycine-specific labeling of proteins, Purushottam, L.; Adusumalli, S. R.; Singh, U.; Unnikrishnan, V. B.; Rawale, D. G.; Gujrati, M.; Mishra, R. K.; **Rai, V.** *Nat. Commun.* **2019**, *10*, 2539. Impact factor: 14.92

Maspecter® toolkit (Patent filed)

The confidence in the precision of bioconjugation required us to address a few limitations of the proteomics-based analysis. In this perspective, we developed Maspecter series products that allow us to detect peptides at attomolar concentrations. Moreover, it provides one of the most efficient toolkits for conjugation site analysis in antibody-conjugates.

[6] Sensitivity booster for mass detection enables unambiguous analysis of peptides, proteins, antibodies, and protein conjugates, Singudas, R.; Reddy, N. C.; **Rai, V.** *Chem. Commun.* **2019**, *55*, 9979-9982. Impact factor: 5.996

Reactivity hotspots (Patent granted)

Till recently, precision engineering of native proteins was considered impractical. Our initial efforts involved understanding and establishing principles to regulate the reactivity and diverse attributes of selectivity in protein bioconjugation. The reactivity hotspot knowledge helped us come up with design principles for Gly-tag and LDM technologies.

[7] Single-site labeling of histidine in proteins, on-demand reversibility, and traceless metal-free protein purification, Joshi, P. N.; **Rai, V.** *Chem. Commun.* **2019**, 55, 1100-1103. Impact factor: 5.996

[8] Single-site labeling of lysine in proteins through a metal-free multicomponent approach, Chilamari, M.; Kalra, N.; Shukla, S.; **Rai, V.** *Chem. Commun.* **2018**, 54, 7302-7305. Impact factor: 5.996

[9] Chemoselective and site-selective peptide and native protein modification enabled by aldehyde auto-oxidation, Purushottam, L.; Adusumalli, S. R.; Chilamari, M.; **Rai, V.** *Chem. Commun.* **2017**, 53, 959-962. Impact factor: 5.996

Additional ADC contribution

[10] Computationally designed antibody-drug conjugates self-assembled via affinity ligands, Gupta, N.; Ansari, A.; Dhoke, G. V.; Chilamari, M.; Sivaccumar, J.; Kumari, S.; Chatterjee, S.; Goyal, R.; Mukherjee, M.; Sarkar, A.; Mandal, S. K. **Rai, V.**; Biswas, G.; Sengupta, A.; Roy, M.; Roy, S.; Sengupta, S. *Nat. Biomed. Eng.* **2019**, 3, 917-929. Impact factor: 18.952