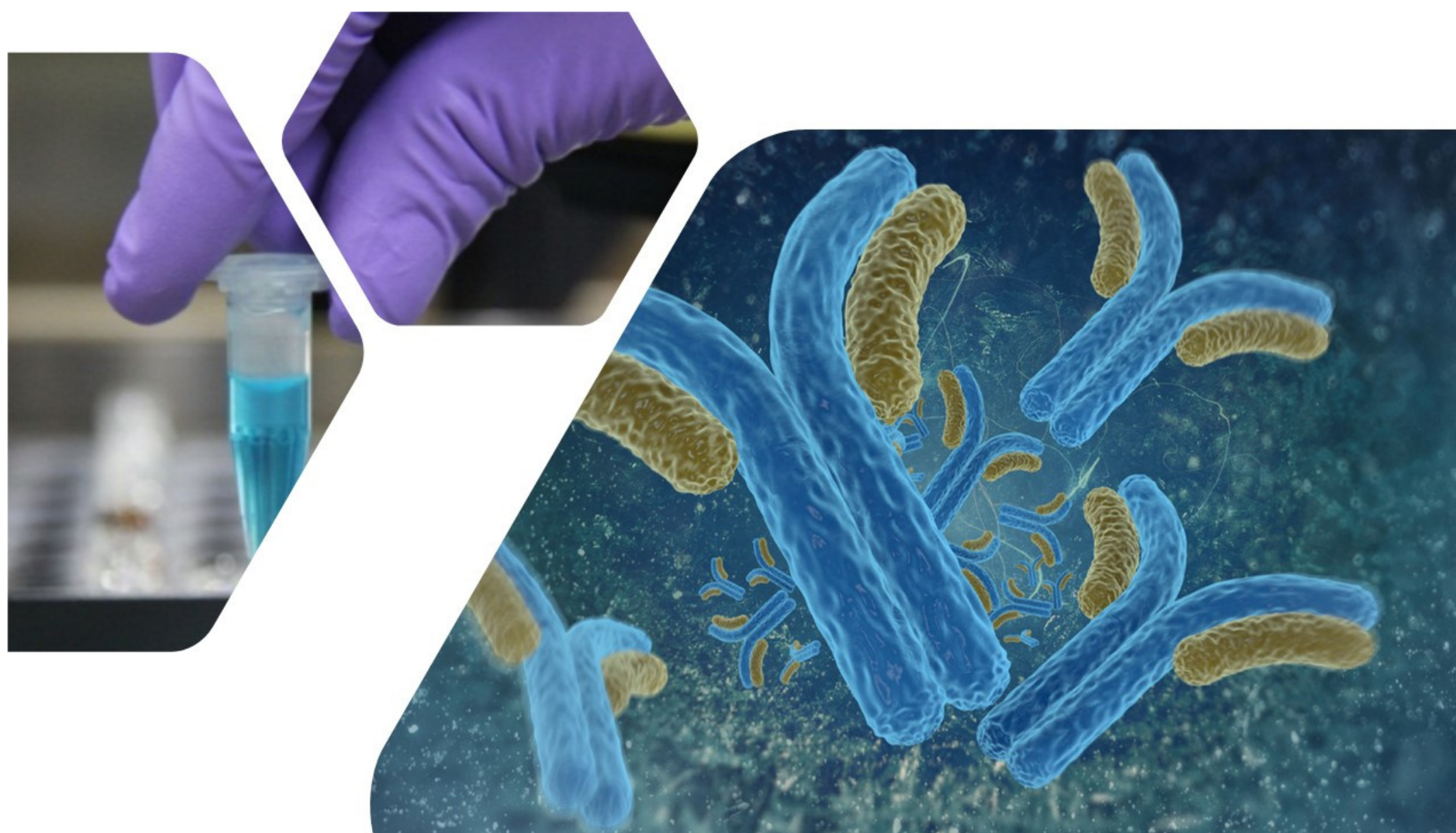




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# Precision chemistry of native proteins enabling biology and medicine



The chemical toolbox for investigating biological systems or enabling therapeutics requires the precise covalent attachment of tags to the proteins. In this perspective, we have been investing efforts to develop chemical technologies that can empower precise control over the site of bioconjugation.

The critical barrier involves the simultaneous deconvolution of multiple challenges associated with reactivity and selectivity. In this perspective, our *DisINtegrate* or *DIN theory* allows us to create new reactivity landscapes on a protein's surface. Overall, it enabled the development of methods for targeting N-terminus,<sup>1</sup> Lys or His hotspots,<sup>2</sup> N-Gly (Gly-Tag<sup>®</sup>),<sup>3</sup> and modular linchpin directed modification (LDM<sup>®</sup>) of His, Lys, and Asp.<sup>4</sup> Some of these technologies address the challenges of homogeneous antibody-drug conjugates (ADCs) for directed cancer chemotherapeutics.<sup>4,5</sup>

The talk would highlight the functional group's preferences while experiencing all the emotions from its social ecosystem. Besides, we will discuss its implications on the new reactivity landscape and precision therapeutics.

#### References and Notes:

- [1] For N-targeting, see: (a) *Chem. Commun.* 2015, 51, 473-476. (b) *Org. Biomol. Chem.* 2018, 16, 9377-9381.
- [2] For reactivity hotspots, see: (a) *Chem. Commun.* 2019, 55, 1100-1103. (b) *Chem. Commun.* 2018, 54, 7302-7305. (c) *Chem. Eur. J.* 2017, 23, 3819-3823. (d) *Chem. Commun.* 2017, 53, 959-962.
- [3] For Gly-Tag, see: (a) *Nat. Commun.* 2019, 10, 2539. (b) *Chem. Sci.* 2020, 11, 13137-13142.
- [4] For LDM and ADC, see: (a) *J. Am. Chem. Soc.* 2018, 140, 15114-15123. (b) *Angew. Chem. Int. Ed.* 2020, 59, 10332-10336. (c) Manuscript under revision.
- [5] For other ADC methods, see: (a) *Nat. Biomed. Eng.* 2019, 3, 917-929. (b) *Chem. Commun.* 2019, 55, 9979-9982.