Synthetic and Medicinal Chemistry for Biologics

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Advances in peptide synthesis allow atom-by-atom control over sequence and structure, enabling the design of therapeutics with unprecedented precision. Building on this foundation, our group has developed a suite of technologies for: 1) chemoselective peptide ligations, 2) site-specific modification of recombinant proteins, and 3) amide-forming bioconjugations that function efficiently at micromolar concentrations. These advances provide streamlined access to atomically-tailor protein therapeutics, – including cytokines and growth factors – engineered for receptor selectivity and conjugations to targeting agents.

In collaboration with Bright Peak Therapeutics, we leveraged our core technology — the α-ketoacid–hydroxylamine (KAHA) ligation — for the GMP production and conjugation of fully synthetic interleukin-2 variants, assembled from four peptide segments prepared by standard Fmoc-SPPS. This campaign establishes chemical protein synthesis as a viable and cost-effective technology for accessing folded, half-life extended therapeutic proteins containing multiple non-canonical amino acid residues.

In parallel, we have expanded the chemical toolbox for protein engineering by developing new chemical and chemoenzymatic approaches for site-specific modification of recombinant proteins and pioneered amide-forming bioconjugations capable of joining folded proteins efficiently under mild conditions, broadening the scope for constructing complex, multispecific therapeutics.