Semisynthetic Study of Glycoprotein Interleukin-6 (IL-6)

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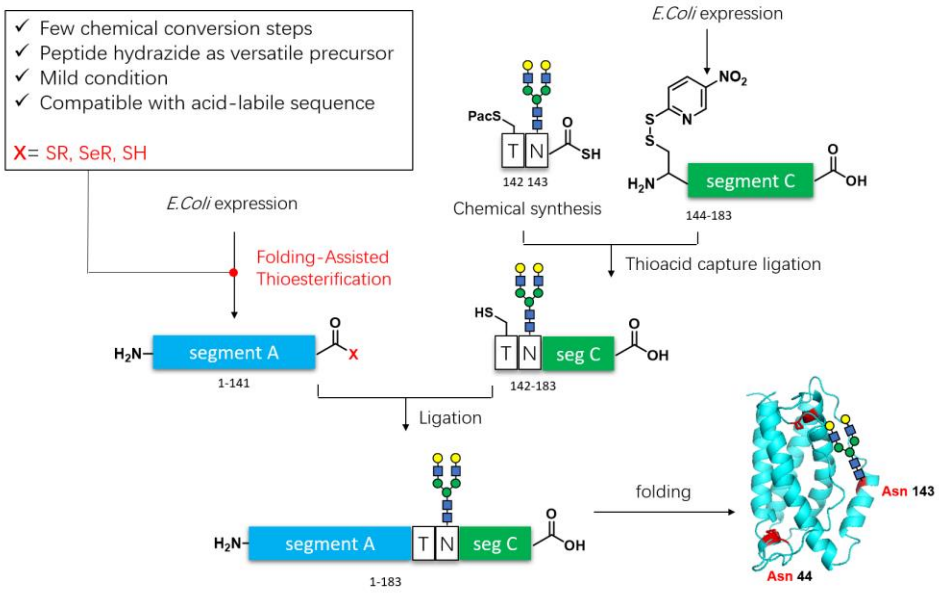
Preparation of glycoproteins having homogeneous oligosaccharides is essential approach for understanding the glycan function at molecular level. However, current mammalian cell expression system is usually not able to yield such homogeneous form. Moreover, total chemical synthesis using solid phase peptide synthesis (SPPS) is time-consuming.

In this research project, we have been establishing a novel semisynthetic strategy without using SPPS in order to obtain homogeneous glycoprotein within a few chemical conversion steps. In this strategy, the challenging expressed-peptide thioesterification of N-terminal segment consist of 141 residues is achieved by a newly developed folding-assisted thioesterification method. In this method, peptide hydrazide derivative is obtained as a versatile precursor that can be utilized for various ligation method. The glycopeptide is prepared by thioacid capture ligation using chemically synthesized asialylglycodipeptide and an expressed peptide.[1] The final ligation step which afford full-length glycosylated IL-6 is examined using thioester, selenoester or thioacid derivative which are prepared via folding-assisted thieosterification.



1) Kota Nomura, Yuta Maki, Ryo Okamoto, Ayano Satoh, and Yasuhiro Kajihara, *J. Am. Chem. Soc.* **2021**, *143*, 10157-10167

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