Semisynthetic study of Interferon-β (IFN-β)

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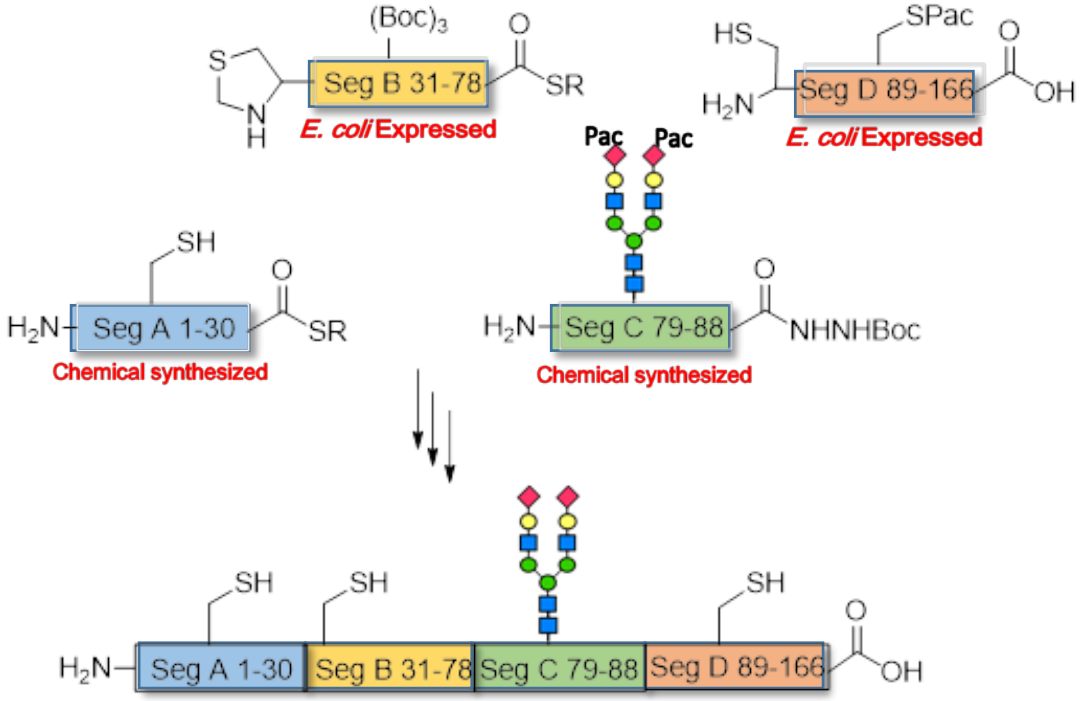
Glycoprotein Interferon-β (IFN-β) is a cytokine having antiviral properties and commonly applied to multiple sclerosis (MS) treatment. Research has shown that the attachment of oligosaccharide greatly contributes to the activity of IFN-β. In order to understand the function of the oligosaccharide on IFN-β, we have worked on efficient preparation of homogeneous IFN-β using semisynthetic methods combining the merits of chemical synthesis and *E. coli* expression.

In this semisynthesis, the full sequence (166 amino acids) was divided into four segments (Figure). Fmoc-HN-Asn(oligosaccharide)-OH was prepared as previously reported,[1] and used for synthesis of the glycopeptide (Seg C). The glycosyl asparagine was sequentially coupled with a nonprotected peptide and Fmoc-Trp(Boc)-OH for the efficient glycopeptide synthesis, instead of typical solid-phase peptide synthesis. Moreover, Seg B and D were prepared in *E. coli* using SUMO tag for efficient expression. Especially, Seg B-thioester was prepared from a peptidyl cysteine by cyanylation of the thiol and following thioesterification.[2] According to peptide ligation chemistry, including native chemical ligation, we successfully synthesized the full-length glyco-polypeptide efficiently. In addition, we currently examine the improved semisynthetic strategy using synthetic γ-mercaptothreonine[3] as a new ligation site. In this presentation, we would like to discuss details of our semisynthesis of IFN-β.



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