One Pot-Chemical Synthesis of Glycoproteins and Their Glycan-Hydration Effect

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The glycosylation of proteins is one of the most abundant posttranslational modifications of proteins. Due to the intrinsic structural complexity, the function of oligosaccharides on glycoproteins is still unclear at a molecular level. We have been studying the function of oligosaccharides on glycoproteins by using homogeneous glycoproteins prepared by chemical synthesis. Our results suggested that the unique hydration of oligosaccharides attenuates the function of glycoproteins[1)]. We hypothesized that the hydration of oligosaccharides affects the molecular recognition of protein moiety of glycoproteins. However, there was no systematic study for the elucidation of the hydration volume of various oligosaccharides on glycoproteins. In order to address this question, we need to prepare a variety of glycoproteins having different oligosaccharides as key probes.

In this study, we set out the synthesis of chemokine glycoprotein CCL1[2)3)] having a variety of oligosaccharide. We newly developed one-pot peptide coupling reactions using peptidyl-2-aminothiazoline (peptide-AT). We found that peptide-AT is interconvertible with peptide-thioester, and thereby enabling regioselective peptide coupling. With the unique reactivity of peptide-AT, we successfully assembled the full length of CCL1 through a sequential peptide coupling reaction in one-pot manner. This synthetic strategy allowed us the efficient preparation of CCL1 having different oligosaccharides. By using the homogeneous glycosyl CCL1, we also conducted the hydrogen deuterium exchange mass spectrometry (HDX-MS) of the resultant glycoproteins to address the hydration region of oligosaccharides on glycoproteins. In this presentation, we would present the detail of the new synthesis and the results of HDX-MS.

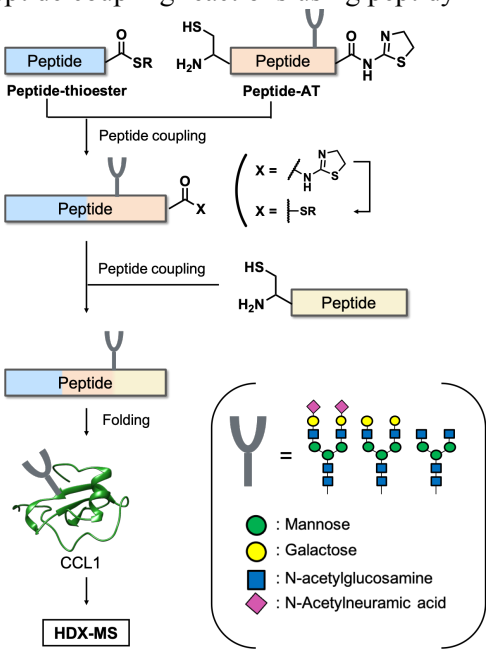

Fig. 1 The synthesis of CCL1 using One-Pot method

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