Glyco-Amino Acid Synthesis and the Effect of Glycosylation on Chemotaxis

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The protein chemokine ligand-5 (CCL5) is naturally produced in the human body and plays a major role in induced chemotaxis (movement of responsive cells to certain environments) of white blood cells to inflammatory sites. Glycosylation is the process of synthesizing a peptide chain with sugars on designated amino acids so as to influence protein interactions and also the potential structure and function differences of the final protein. Successfully glycosylated CLL5 proteins may alter the level of chemotaxis and therefore offer a solution to conditions like inflammatory diseases. Here, I synthesized a glycosylated amino acid used in protein synthesis called N-acetylgalactoseamine-serine (GalNac-serine). I prepared the glucose ring first by protecting the exposed hydroxyl groups and activating the sugar. The carboxylate group of the Fmoc-Ser was protected with a tert-butyl (tbu) group. I coupled the activated sugar with Fmoc-Ser-Otbu and reduced the azide. The final step was removing the tbu group. The organic synthesis of GalNac-Serine had an average yield of 65% per step and produced 1.208 g, 20.8% more than the target mass. Nuclear magnetic resonance (NMR) revealed a 96% pure final product. As the next step in my future direction, GalNac-serine will be used to glycosylate eleven discrete samples of CCL5 that will be analyzed alongside a non-glycosylated control sample. Protein folding and structure will be noted, and CCL5 will be studied in a white blood cell environment. I will then be able to conclude a relationship between the distinct glyco-proteins and the induced chemotaxis effect.