Probing the effects of glycosylation on peptide and protein activity through chemical synthesis

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Glycosylation is the most common co- and post-translational modification of polypeptides, with over 50% of human proteins predicted to display covalently bound glycans. Glycosylation has been shown to mediate an array of biological recognition events in all domains of life. Additionally, a number of recently approved biopharmaceuticals contain carbohydrate chains (or carbohydrate mimics) that are critical for activity and/or stability.[1] The non-templated enzymatic nature of the glycosylation process leads to heterogeneous mixtures of isoforms when glycopeptides and glycoproteins are isolated or produced in recombinant expression systems, thus hindering the ability to study how glycosylation influences function in a meaningful way. This has led to significant demand for new tools and technologies to facilitate access to homogeneous glycopeptides and glycoproteins to interrogate the role of individual carbohydrate modifications on structure and function.

Our lab has recently developed a number of synthetic technologies to access homogeneously glycosylated peptides and proteins for structure-function studies.[2,3] This talk will highlight the synthesis and evaluation of glycopeptide and glycoprotein hormones[4,5] and glycoproteins from Gram negative bacteria.

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