

## INTRODUCTION TO SPECIAL ISSUE

## Chemical Glycobiology

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The postgenomic era is undergoing a major paradigm shift from identifying mutations in individual genes to exploring functions of gene products at molecular, cellular, organismal and population levels. As stated by Craig Venter and coworkers, “The finding that the human genome contains fewer genes than previously predicted might be compensated for by combinatorial diversity generated at the level of *posttranslational modifications*” (Venter et al. 2001). Among all types of posttranslational modifications, glycosylation is structurally the most complex one. Most posttranslational modifications involve the addition of a monomeric co-factor (phosphate, methyl, acetyl, etc.) to an amino acid side chain. However, cell surface glycosylation involves the stepwise addition of monosaccharide building blocks to form complex oligomeric structures that can either be linear or branched with further modifications such as phosphorylation, sulfation and acetylation. These factors make glycosylation a unique posttranslational modification that may encode information for specific molecular recognition events. The same reasons that make glycosylation a fascinating topic for biological investigations also thwart efforts to elucidate their biological functions. Without tools to decipher the glycan code at the molecular level, it is difficult to appreciate their functions in cellular systems.

In this special issue of *Glycobiology*, four young investigators review recent advances in the field of chemical glycobiology with a focus on the development of chemical tools that are expected to serve as a major driving force to understand glycoscience at a molecular level.

Since Reutter and Bertozzi demonstrated that unnatural monosaccharides can be incorporated into cellular glycoconjugates through the cells’ glycan biosynthetic machinery, cell surface oligosaccharide engineering has become a very active area of research. Recent developments in metabolic and enzymatic approaches for this endeavor are reviewed by Nischan and Kohler. The discussion is centered on three aspects, namely (1) applying these tools to characterize changes of glycosylation patterns during immune cell activation and tumor progression, (2) cell surface glycan modification to direct stem cell trafficking and (3) unnatural monosaccharide-based inhibitor to remodel glycosylation patterns in cellular systems and murine models.

In addition to the development of chemical and enzymatic tools to modify glycans on the cell surface, chemists have designed and synthesized structurally well-defined glycopolymers to probe cell surface glycan–receptor interactions. The review by Huang and Godula summarizes recent advances in this area and highlight the use of glycopolymers to control neural differentiation and B-cell signaling. Applications of glycan–peptide and glycan–nucleic acid conjugates are also discussed.

The heterogeneity of naturally occurring glycans remains a major hurdle for glycobiologists in their quest to determine the roles of glycans in modulating the function of anchored proteins. Tanaka and coworkers review bioorthogonal approaches to conjugate structurally well-defined mono- and oligosaccharides to proteins. Using homogenous saccharides synthesized via chemoenzymatic approaches, the pivotal role of glycans in controlling the serum stability and organ distribution of proteins can be studied.

Glycans often interact with cell surface receptors in a multivalent fashion. Likewise, antibody–glycan recognitions follow the same binding principle. In the final review of this special issue, Krauss provides an overview of recent structural biology studies that have shed light on the importance of multivalent interactions with clustered glycans and glycopeptides in achieving specificity by HIV and dengue-neutralizing antibodies. An appreciation of these interactions is key to the design of vaccines against these deadly human pathogens.

In conclusion, glycoscience is no longer a Cinderella field due to the development of new synthetic methods and chemical tools. Combining these new tools with genetic, structural and biochemical approaches, glycobiologists are equipped to address the molecular mechanisms by which glycans exert their functions in the context to human health and disease.

## References

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