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# Editorial: Glycotherapeutics: Design, synthesis, function and biomedical application of agents emerging from glycochemistry and glycobiology

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## Editorial on the Research Topic

[Glycotherapeutics: Design, synthesis, function and biomedical application of agents emerging from glycochemistry and glycobiology](#)

Post-translational glycosylation is a non-template driven process for the addition of carbohydrates, or glycans, to biomolecules such as protein and lipids. It is well recognized that glycosylation impacts many cellular processes including, but not limited to, protein folding, trafficking, receptor binding, signaling, inflammation, and cell-to-cell/matrix adhesion (Varki 2017). Additionally, glycans can be used in the targeting of drugs in diseases such as cancer (Diniz et al., 2022) and lysosomal storage disorders (Do et al., 2019) as well as modulating pharmacokinetics and immunogenicity of therapeutic proteins and antibodies (Liu 2015; Archer et al., 2022; Dammen-Brower et al., 2022).

The goal of this Research Topic was to assemble a collection of articles highlighting recent advancements pertaining to diagnostic tools and therapeutics utilizing multidisciplinary approaches in glycobiology and glycochemistry. Collectively, four articles submitted by 21 experts in glycoscience were peer-reviewed and accepted for publication in this Research Topic to emphasize the importance of glycans in human health and disease, in addition to presenting rapidly evolving technologies used in the analysis of carbohydrate-modified molecules and the enzymes that synthesize or degrade them.

A review article by Loaeza-Reyes et al. provides a comprehensive overview of protein N-linked and O-linked glycosylation and their implications in cardiovascular function and disease, including an analysis of cardiovascular

disease risk factors associated with aberrant *N*-glycosylation and the dynamic role of the *O*-GlcNAc modification in inflammation. With more than 7,800 proteins modified in humans, *O*-GlcNAcylation is a critical modulator of signaling pathways in health and diseases (Wulff-Fuentes et al., 2021). Taking an analytical approach, Burt et al. provide a review of this dynamic modification and strategies to elucidate *O*-GlcNAc-modified proteins using high performance liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS). The glycosidic bond between GlcNAc and serine or threonine residues is inherently labile, thus careful MS fragmentation strategies must be taken into consideration in order to accurately detect *O*-glycopeptides. While the mass spectrometer cannot discern the two HexNAc stereoisomers, GlcNAc and GalNAc, the authors summarize efforts in the literature to accurately identify the correct stereoisomers based on the ratio of fragment ions produced from the respective glycans. Additionally, Mukherjee et al. contributed a review article describing synthetic approaches to stereoselective chemical *O*-glycosylation reactions, which can be extremely challenging. This valuable summary of methods will aid the synthetic chemist in deriving a strategy for synthesizing target glycans with defined glycosidic linkages, including 1,2-*cis*, 1,2-*trans* and 2-deoxy-glycosides. Finally, a research article by Howlader et al. studied human neuraminidase enzymes and their roles in transmigration using an *in vitro* system. Here, the authors investigated the pharmacological inhibition of the NEU1, NEU3, and NEU4 isoenzymes. They propose these enzymes are positive regulators of transmigration and are potential targets for anti-inflammatory approaches.

In summary, within this Research Topic we sought to highlight the recent advancements in Glycoscience and how they can be utilized for therapeutic approaches to human diseases. We hope this collection of articles will be of interest to the broader scientific community and facilitate further discussion.

## References

- Archer, E. J., Gonzalez, J. C., Ghosh, D., Mellins, E. D., and Wang, T. T. (2022). Harnessing IgG Fc glycosylation for clinical benefit. *Curr. Opin. Immunol.* 77, 102231. doi:10.1016/j.coi.2022.102231
- Dammen-Brower, K., Epler, P., Zhu, S., Bernstein, Z. J., Stabach, P. R., Braddock, D. T., et al. (2022). Strategies for glycoengineering therapeutic proteins. *Front. Chem.* 10, 863118. doi:10.3389/fchem.2022.863118
- Diniz, F., Coelho, P., Duarte, H. O., Sarmento, B., Reis, C. A., and Gomes, J. (2022). *Glycans as Targets for Drug Delivery in Cancer*, 14. *Cancers* (Basel).
- Do, H. V., Khanna, R., and Gotschall, R. (2019). Challenges in treating pompe disease: An industry perspective. *Ann. Transl. Med.* 7, 291. doi:10.21037/atm.2019.04.15
- Liu, L. (2015). Antibody glycosylation and its impact on the pharmacokinetics and pharmacodynamics of monoclonal antibodies and Fc-fusion proteins. *J. Pharm. Sci.* 104, 1866–1884. doi:10.1002/jps.24444
- Varki, A. (2017). Biological roles of glycans. *Glycobiology* 27, 3–49. doi:10.1093/glycob/cww086
- Wulff-Fuentes, E., Berendt, R. R., Massman, L., Danner, L., Malard, F., Vora, J., et al. (2021). The human *O*-GlcNAc database and meta-analysis. *Sci. Data* 8, 25. doi:10.1038/s41597-021-00810-4

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## Conflict of interest

MS was employed by the Amicus Therapeutics Inc. and holds equity in the company in the form of stock-based compensation.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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