Enzymatic Acceptor-Mediated Glycosylation for the Synthesis of Fucosylated Oligo-LacNAcs and GAA-7 Glycan

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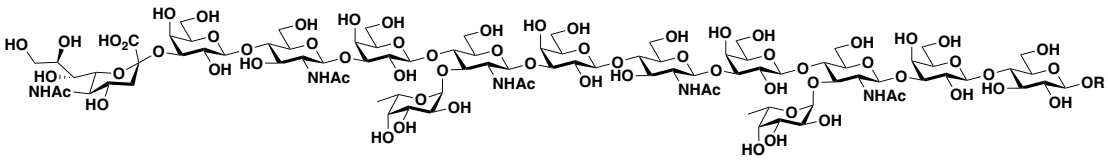
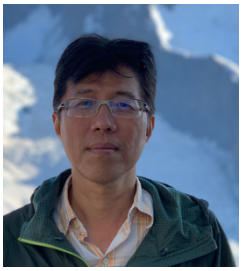
Fucose in fucosylated glycans is primarily assembled at multiple sets of *N*-acetyllactosamine (LN) and lacto-*N*-biose (LNB) units. The synthesis of these compounds is difficult due to the diversity of fucose position on complex glycans. A promising strategy is to perform enzymatic fucosylation with oligosaccharide backbones because the method is stereoselective and synthetically efficient. Herein, we developed a general enzymatic strategy to perform site-specific fucosylation on poly LN or LN/LNB hybrid backbones. In our strategy, TFA protected glucosamine (GlcNTFA) served as the GlcNAc substituent and was incorporated into the LN/LNB chain. The TFA group was then transformed to a butyloxycarbonyl (Boc) group and the resulting GlcNBoc can be the acceptor for bacterial galactosyltransferases but cannot be recognized by fucosyltransferase. Thus, enzymatic fucosylation can only occur specifically at GlcNAc sites of GlcNHBoc-containing poly LN/LNB. We demonstrated the feasibility of this strategy by efficiently synthesizing myeloglycans (dodecasaccharides) and internal/terminal fucosylated human milk oligosaccharides. This approach offers a solution to bypass complex chemical glycosylations and control the selectivity of enzymatic fucosylations. Thus, the method shows significant potential for the future synthesis of branched glycans, such as *N*-glycans and *O*-glycans. The developed strategy was also applied on the synthesis of the glycan moiety of GAA-7.



Structure of VIM-2 glycan

Reference
[1] Tseng, H.-K.; Wang, H.-K.; Wu, C.-Y.; Ni, C.-K. *ACS Catalysis*, **2023**, *13*, 10661.
[2] Anwar, M. T.; Kawade, S. K. et al. *Eur. J. Med. Chem.* **2022**, *232*, 114146.
[3] Tseng, H.-K.; Su, Y.-Y.; Chang, T.-W. *Chem. Commun.* **2021**, *57*, 3468.
[4] Li, P.-J.; Huang, S.-Y.; Chiang, P.-Y et al. *Angew. Chem. Int. Ed.* **2019**, *58*, 11273.



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