

ARE THERE SUGARS IN BACTERIA? WHAT CAN WE DO WITH THEM?

Suvarn S. Kulkarni

Department of Chemistry, Indian Institute of Technology Bombay,
Powai, Mumbai-400076, India
suvarn@chem.iitb.ac.in

Bacterial glycans are often comprised of rare D and L deoxy amino sugars, which are not present on the human cell surface. This peculiar structural difference allows discrimination between the pathogen and the host cell and offers avenues for target-specific drug discovery and carbohydrate-based vaccine development [1]. However, such complex glycans cannot be isolated with sufficient purity in acceptable amounts, and therefore chemical synthesis is a crucial step toward the development of these products [2,3]. We recently established short and convenient methodologies for the synthesis of orthogonally protected bacterial D and L-deoxy amino hexopyranoside and glycosamine building blocks starting from easily available D-mannose and L-rhamnose [4,5]. The one-pot protocols rely on highly regioselective nucleophilic displacements of triflates. These procedures have been applied to the synthesis of various conjugation-ready bacterial glycans [6-8] as well as zwitterionic [9] oligosaccharides. The azide containing sugars also enabled metabolic oligosaccharide engineering studies [10] that led to discovery of selective inhibitors of glycan biosynthesis [11]. In this talk I will present our recent results on the total synthesis of highly complex and densely functionalized bacterial glycans and the application of rare sugars in selective detection and disarming of pathogens. The synthetic oligosaccharides provide valuable epitopes for immunological studies aimed at vaccine development.

References:

1. Dube, D.H.; Champasa, K.; Wang, B. *Chem. Commun.* **2011**, 47, 87-101.
2. Kulkarni, S. S.; Wang, C. C.; Sabbavarapu, N. M.; Podilapu, A. R.; Liao, P. H.; Hung, S. C. *Chem. Rev.* **2018**, 118, 8025–8104.
3. Emmadi, M.; Kulkarni, S. S. *Nat. Prod. Rep.* **2014**, 31, 870-879.
4. Emmadi, M.; Kulkarni, S. S. *Nature Protocols* **2013**, 8, 1870-1889.
5. Sanapala, S. R.; Kulkarni, S. S. *J. Am. Chem. Soc.* **2016**, 138, 4938–4947.
6. Behera, A.; Rai, D.; Kulkarni, S. S. *J. Am. Chem. Soc.* **2020**, 142, 456-467.
7. Rai, D.; Kulkarni, S. S. *Org Lett* **2023**, 25, 1509-1513.
8. Biswas, S.; Ghotekar, B. K.; Kulkarni, S. S. *Org. Lett.* **2021**, 23, 6137–6142.
9. Puri, K.; Kulkarni, S. S. *Comms. Chem.* **2024**, 7, 204.
10. Clark, E. I.; Emmadi, M.; Krupp, K. L.; Podilapu, A. R.; Helble, J. D.; Kulkarni, S. S.; Dube, D. H. *ACS Chem. Biol.* **2016**, 11, 3365-3373.
11. Williams, D. A.; Pradhan, K.; Paul, A.; Olin, I. R.; Tuck, O. T.; Moulton, K. D.; Kulkarni, S. S.; Dube, D. H. *Chem. Sci.* **2020**, 11, 1761-1774.