Synthesizing a Library of Hyperbranched Glycopolymers via RAFT Polymerization for Human Norovirus Inhibition

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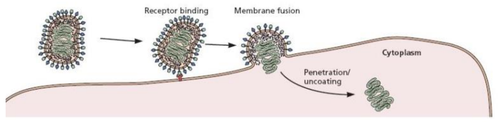
GlycoMIP NSF Materials Innovation Platform

Background

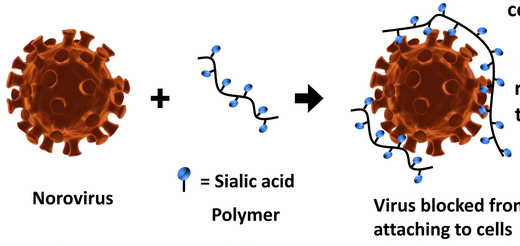
Overview of Human Norovirus (HNV)

- Every year HNV is responsible for **700 million** infections and more than **200,000** deaths
- Low infectious doses (**~1000** viral particles), comparable to other infectious viruses (i.e., influenza, COVID-19)
- Viral shedding can occur anywhere from 2 to 8 weeks; for immunocompromised patients it can be a scale of months/years
- Genetically diverse: 10 genogroups and 49 genotypes (HNV is found in GI, GII, and GIV) which can pose problems for the development of broad antiviral or vaccine candidates
- HNV infections not fully understood: **(1)** lack of long-term immune protection, **(2)** some individuals are less susceptible to infections of specific strains
- Currently there are no vaccines or antivirals on the market



Hassan, E.; Baldridge, M. T., *Mucosal Immunol.* **2019,** *12* (6), 1259-1267.

In the body, HNV will bind to bile salts, or sialic acid, heparan sulfate, and histo-blood group antigens covering the surface of cells. Our goal is to replicate the cell membrane, a surface covered by glycans, by synthesizing materials that contain multiple receptors (e.g., sialic acid) along the polymer backbone to entice the virus.



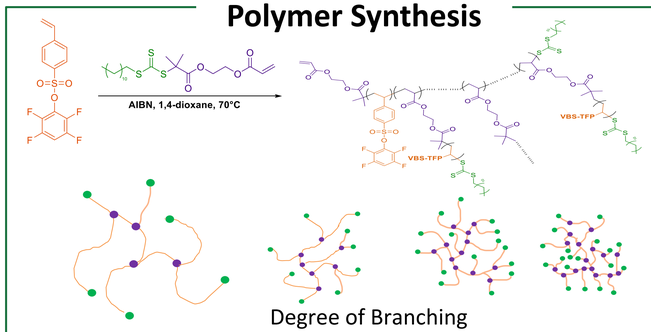
Bianculli, R. H.; **Mase, J. D.**; Schulz, M. D., *Macromolecules* **2020,** *53* (21), 9158-9186.

Research Goals

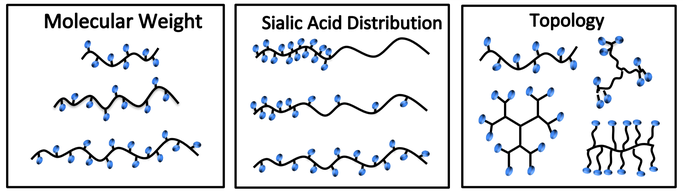
(1) Synthesize protected sialic acids via chemical synthesis
(2) Synthesize histo-blood group antigens (HBGAs) via automated glycan assembly (**GlycoMIP**)
(3) Synthesize hyperbranched polymers tailored for terminal placement of sialic acid or HBGAs
(4) Prepare a library of polymers with varying molecular weights and degrees of branching to investigate optimal antiviral inhibition

Design

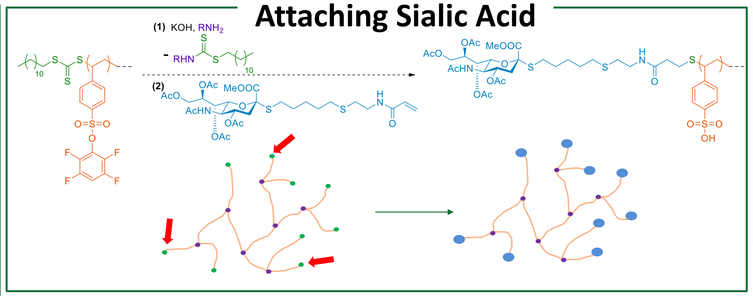
Polymer Synthesis



By varying the degree of branching, we can change the amount of sialic acid we can bind to the polymer.

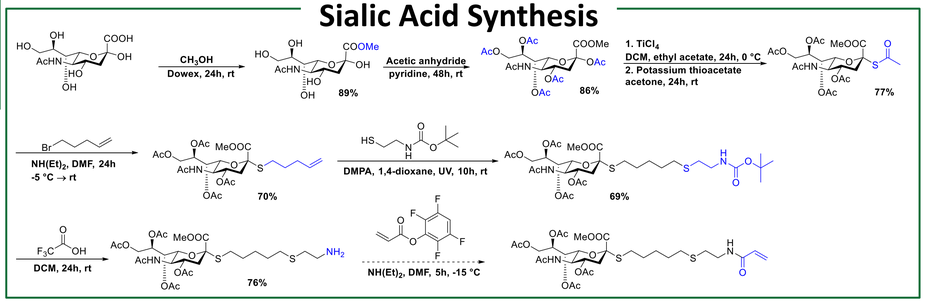


Attaching Sialic Acid

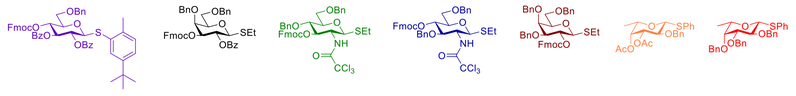


The final synthetic steps require the deprotection of various protecting groups on the sialic acid and the removal of tetrafluorophenyl groups. Similar chemistry can then be done to HBGAs when attaching them to our materials.

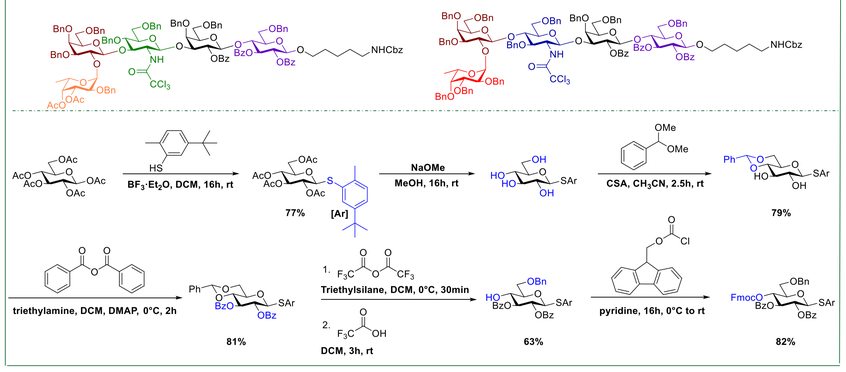
Sialic Acid Synthesis



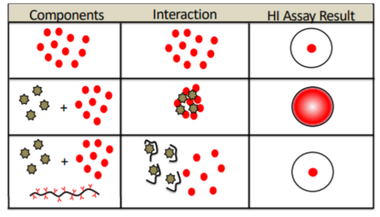
HBGA Synthesis



Automated Glycan Assembly



Future Work



- Develop **broad-spectrum** antiviral materials. Sialic acids bind a wide variety of viruses: coronaviruses, human parainfluenza, adenoviruses, orthoreoviruses, bovine enterovirus
- Investigate other glycans as viral inhibitors including mannose 6-phosphates

- Synthesize HBGA-containing materials to apply towards **bacteria** including *H. pylori* (peptic ulcers) and *E. cloacae* (pneumonia)
- Continue investigating the roles different parameters such as **polymer architecture** and **glycan structure** have on improving a polymer's antiviral potency by synthesizing a large library of glycomaterials

Acknowledgement

This work was supported by GlycoMIP, a National Science Foundation Materials Innovation Platform funded through Cooperative Agreement DMR-1933525.