Carbohydrate Polymers for Cell-Surface Engineering

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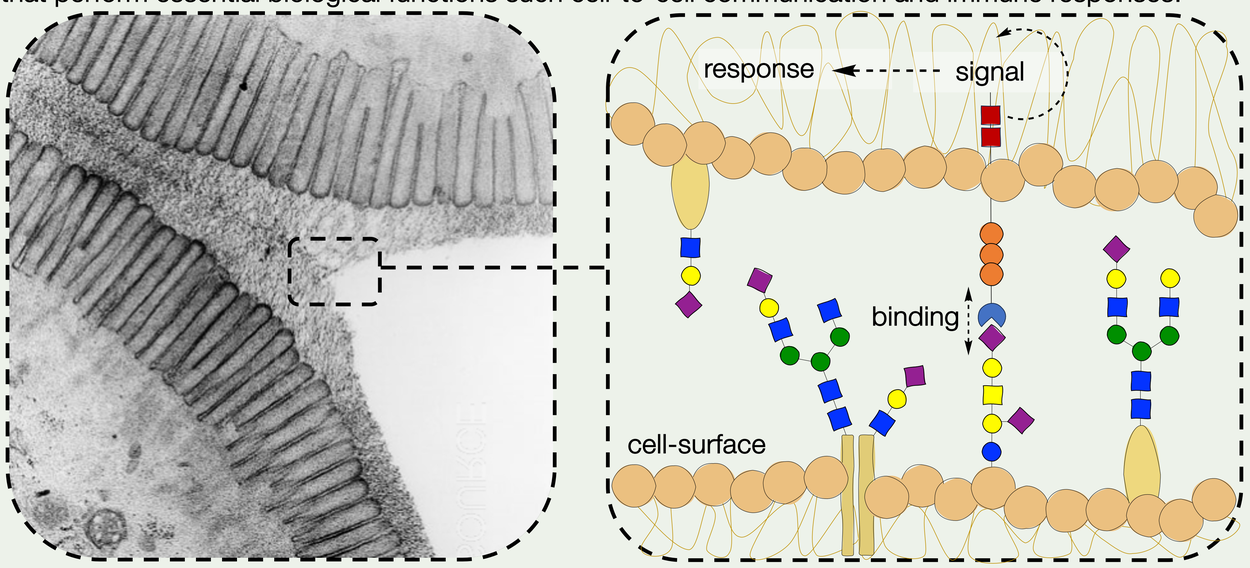
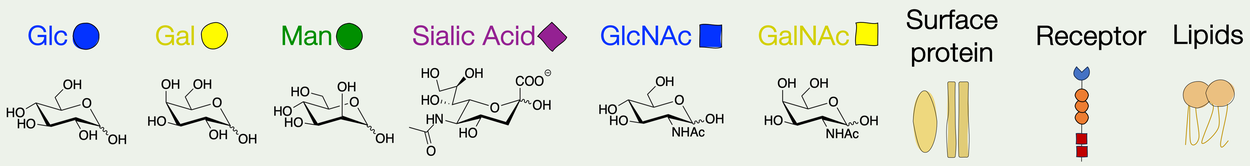
Background

The surface of all mammalian cells are coated with a dense layer of carbohydrates called glycans that perform essential biological functions such cell-to-cell communication and immune responses. [1]





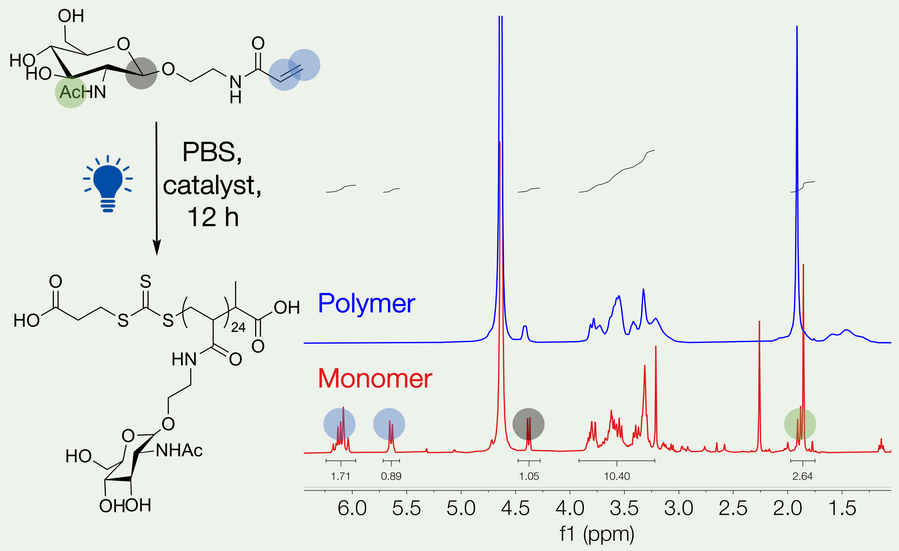
Glycan functions are sequence-defined by 10 monosaccharides and architectural complexity.

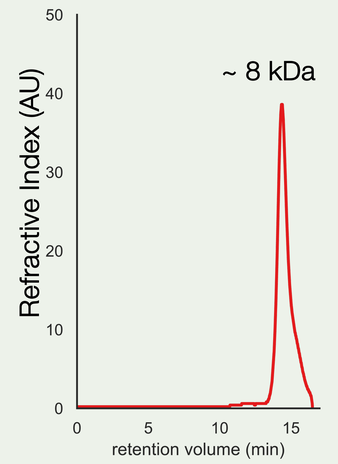
Motivation and Objective

- Glycans are not encoded in the genome and cannot be expressed using genetic strategies [2]
- Our goal is to develop a synthetic route to access sequence-defined glycan materials for immune cell-surface engineering to explore glycan structure-function relationships in biology [3]

Results

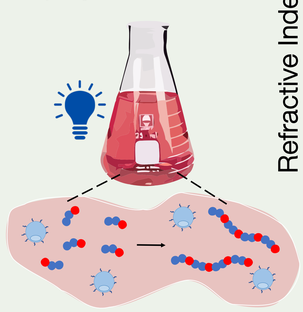
Characterization using 1H-NMR and aqueous Size Exclusion Chromatography

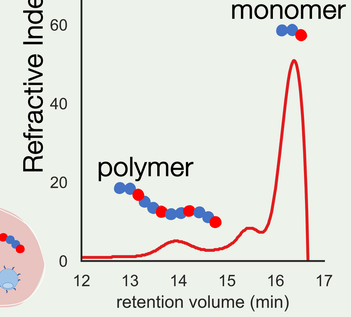




Cytocompatible reaction conditions were screened with a PEG-based monomer to ensure minimal light irradiation and suitable polymer molecular weights (MW)

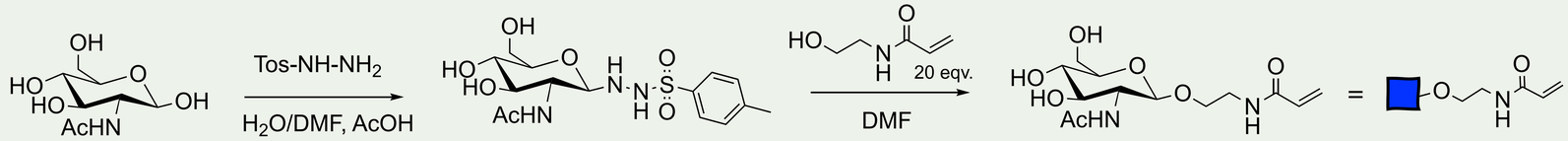
No.	[Monomer]	[Initiator]	[Catalyst]	Irradiation time	O_2	MW	Est. % Conversion
1	80	1	0.015	12 h	Y	-	-
2	80	1	0.015	12 h	N	25 kDa	71%
3	80	1	0.015	1 h	N	19 kDa	38%
4	80	1	0.015	10 min	N	-	-
5	80	0.25	0.003	10 min	N	18 kDa	20%
6	80	0.5	0.0015	10 min	N	18 kDa	55%
7	80	0.5	0.003	10 min	N	18 kDa	35%
8	80	0.75	0.003	10 min	N	18 kDa	70%



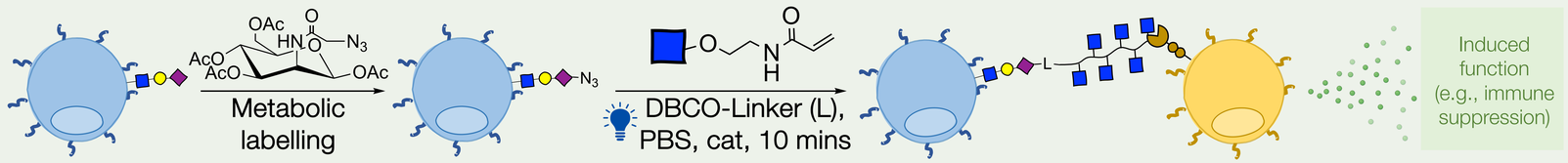


Synthesis & Methods

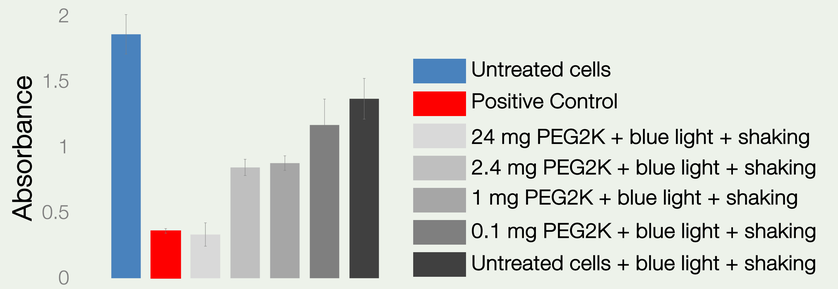
A synthesis was developed starting from the monosaccharide Glucosamine (GlcNac), the first building block of many glycan structures, to obtain glycan-based vinyl monomers suitable for light-initiated polymerization.



Cell-surface glycans will be labelled with azide and clicked together to a polymer chain linker. Next, monomers will be polymerized in the cell suspensions and grafted to the linker affording dense displays of glycan-based polymer on native cell-surface glycans.



A metabolic toxicity assay was conducted on PEG-based monomer to determine the maximum tolerated dose for Jurkat T cells.



Future Directions

Optimized polymerization conditions will be applied to glycan-based monomers towards the development of technology to engineer the surface of live cells with polymers.

References and Acknowledgments

[1] Duan, S.; Paulson, J. C. Siglecs as Immune Cell Checkpoints in Disease. Annual Reviews Immunology (2020). 38: 365 – 395. [2] Seeberger, P. H., & Overkleeft, H. S. Chemical Synthesis of Glycans and Glycoconjugates. Essentials of Glycobiology (2022). 3, 53· [3] Critcher, M., O'Leary, T., & Huang, M. L. Glycoengineering: scratching the surface. Biochemical Journal (2021). 478(4): 703-719.

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