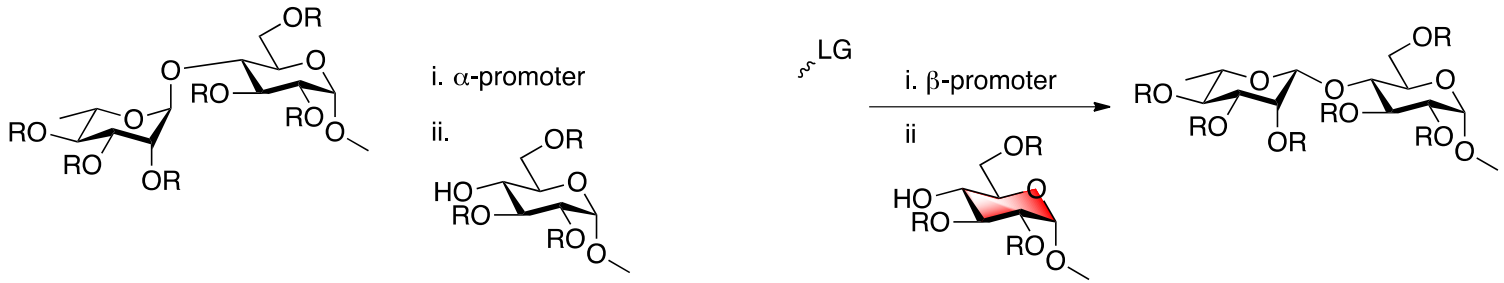
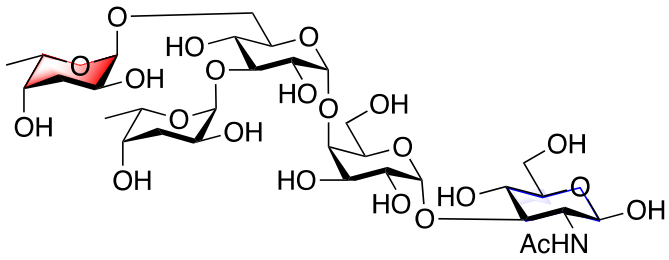
Common Fund Research in the Bennett Group: Reagent Controlled Glycosylation (U01GM120414-01)

Developing Chemical Promoters that Permit Absolute Control Over the Stereochemical Outcome of Glycosylation Reactions:



These Promoters will Make Oligosaccharide Construction Similar to Peptide Synthesis:



Rapid Construction of Oligosaccharides for Analytical Standards and Therapeutic Development!

https://commonfund.nih.gov/Glycoscience/fundedresearch#

Refinement and implementation of the automated oligosaccharide synthesizer (U01GM120673, 2016-)

Alexei V. Demchenko, Keith J. Stine, University of Missouri - St. Louis
& Cristina De Meo, Southern Illinois University, Edwardsville

detector

column

solid support

glycosyl acceptor

pump

activators

autosampler

recirculation chamber

solutions for washing and deprotection

diversification sites

diversification sites

Human milk oligosaccharides and other glycans

retrosynthetic analysis

large-scale preparation of

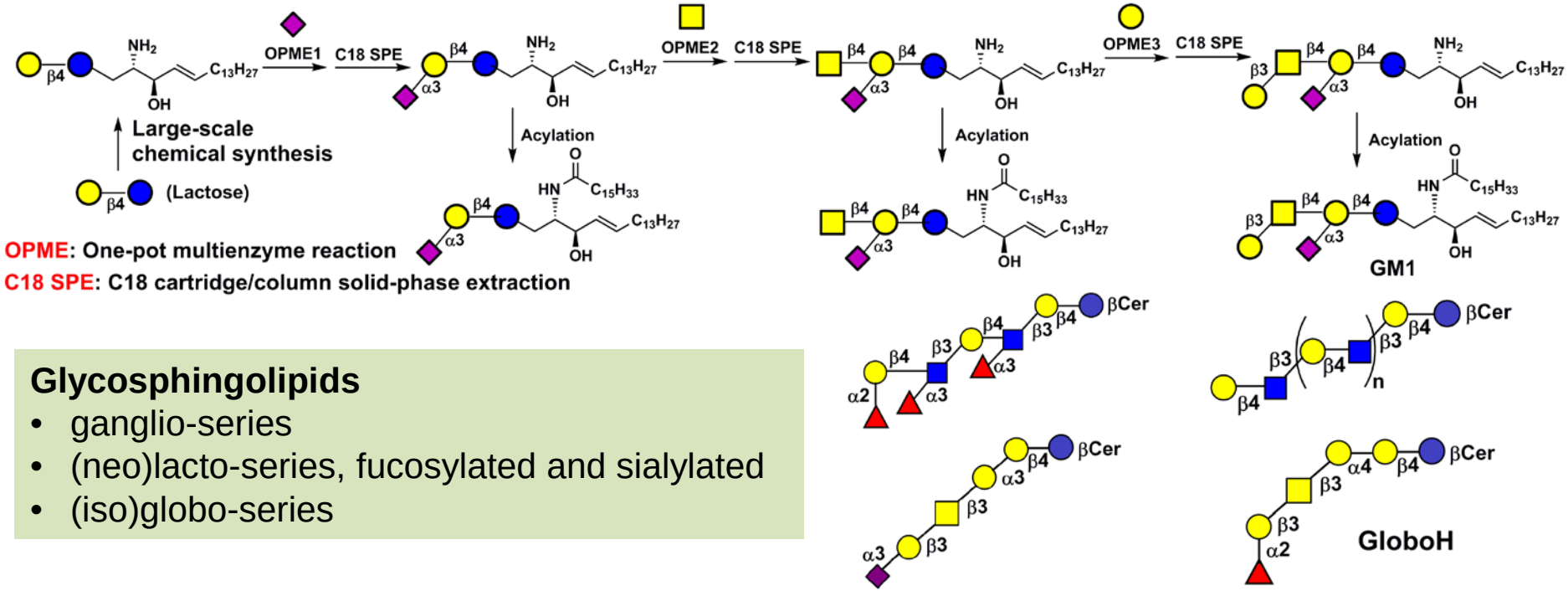
generic building blocks

Specific building blocks

Facile chemoenzymatic synthesis and purification of glycolipids

NIH Common Fund Glyco-science Program (U01GM120419)

Xi Chen, U. of California-Davis, xiichen@ucdavis.edu, http://chenglyco.faculty.ucdavis.edu/
Peng G. Wang, Georgia State U., pwang11@gsu.edu, http://lithium.gsu.edu/faculty/PWang/



Glycosphingolipids

- ganglio-series
- (neo)lacto-series, fucosylated and sialylated
- (iso)globo-series

Goal: To allow non-specialists to synthesize, functionalize, purify, and study glycosphingolipids

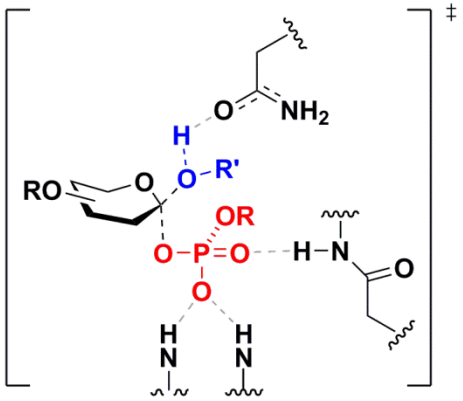
- Identify stable storage conditions for enzymes and reagents
- Assemble OPME enzyme and reagent kits
- Optimize reaction and purification conditions
- Establish protocols for OPME synthesis and C18 cartridge/column purification
- Cross-validation
- For more information, see http://chenglyco.faculty.ucdavis.edu/glycosphingolipids/

Glc
Gal
GlcNAc
GalNAc
Fuc
Sia

Jacobsen Group

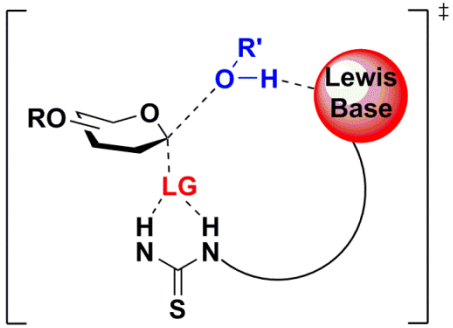
Developing Catalysts for Selective Glycosylation

Nature's solution:



• Selectivity through stereospecificity

Our approach:

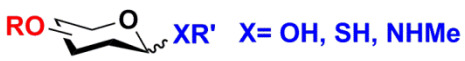


• Mild reaction condictions through dual-activation strategy

• Catalyst-promoted stereospecificity

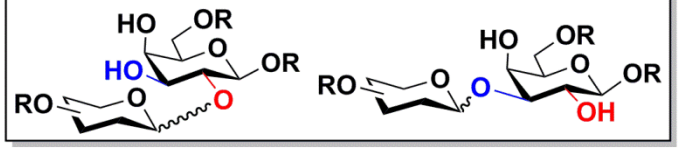
New strategy enables:

•Broad nucleophile, electrophile scope

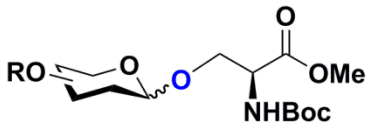


R= OBn, Me, OAc, NHAc, N_3

•Catalyst control of multiple reactive sites

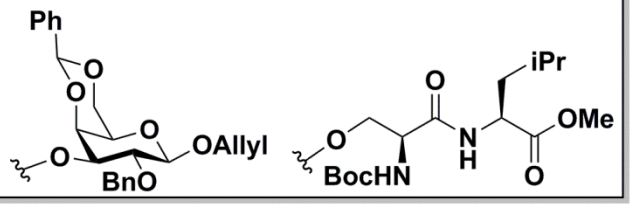


•High anomeric selectivity, efficient reactivity



>20:1 β:α , < 4 hours

•High functional group compatibility

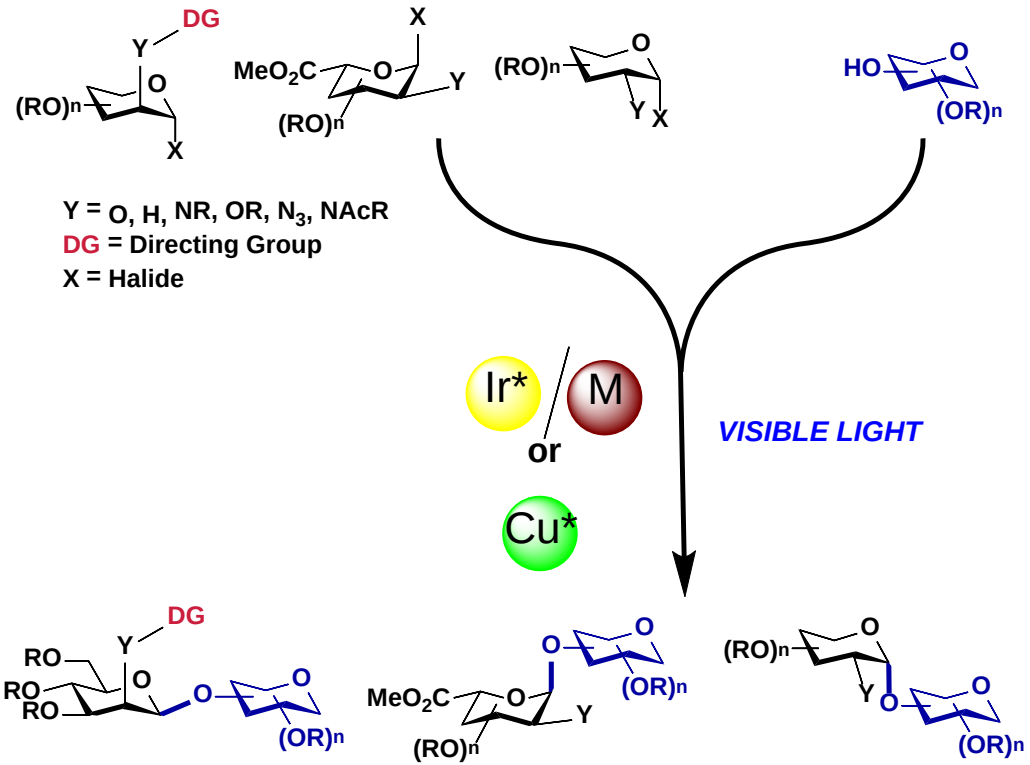


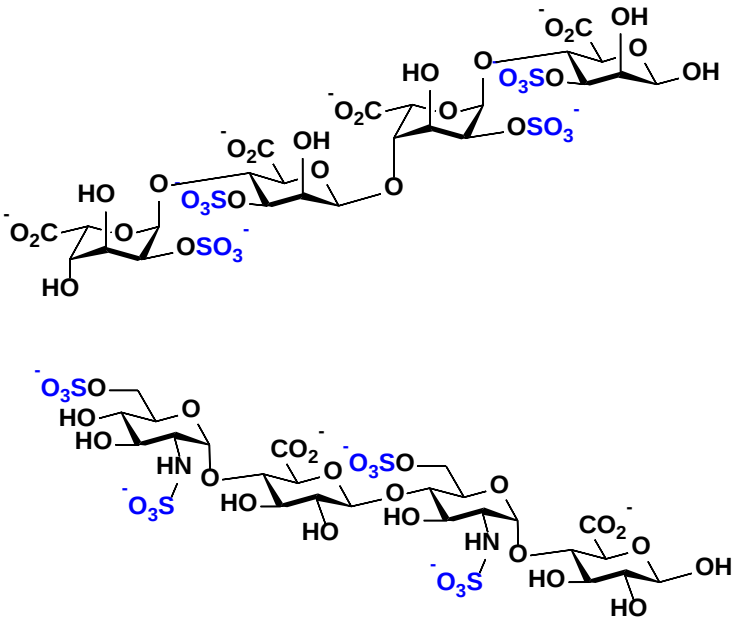
Park, Y; Harper, K. C.; Kuhl, N.; Kwan, E. E.; Liu, R. Y.; Jacobsen, E. N. *Science* **2017**, *355,* 162.

Kwan, E. E.; Park, Y.; Besser, H. A.; Anderson, T. L.; Jacobsen, E. N. *J. Am Chem. Soc.* **2017**, *139*, 43

NIH Common Fund Research in the Nguyen Group: Stereoselective 1,2-Cis Glycosylation

Developing predictable and stereoselective 1,2-cis glycosylation reactions via either dual catalytic photoredox catalysis or photoinduced copper catalysis





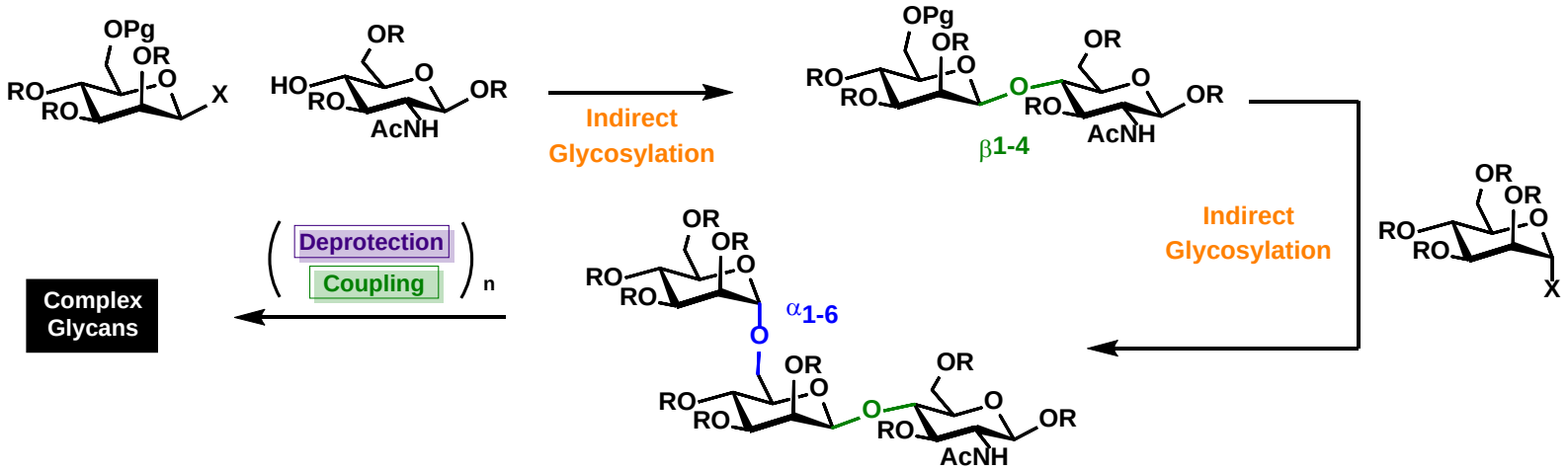
Rapid and stereoselective synthesis of bioactive oligosaccharides for analytical standards and therapeutic applications

NIH-U01 GM120293
https://commonfund.nih.gov/Glycoscience

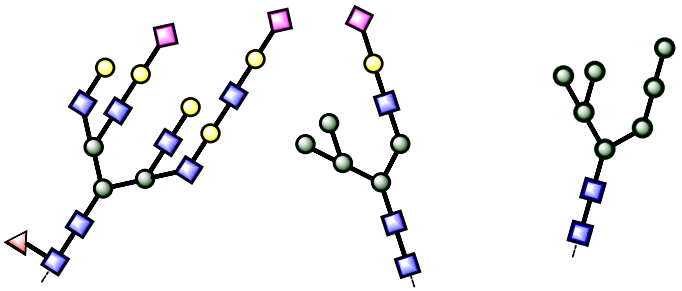
Hien M. Nguyen (hien-nguyen@uiowa.edu)
University of Iowa
https://nguyenresearchgroup.lab.uiowa.edu/

NIH Common Fund Research in the Brichacek Group: Novel Glycosylation Mechanisms

Indirect Glycosylation Methods to Facilitate More Efficient and Selective Couplings



Enable access of oligosaccharides of defined sequence, branching, and stereochemistry on demand to a diverse range of biomedical researchers.



NIH-U01GM120410

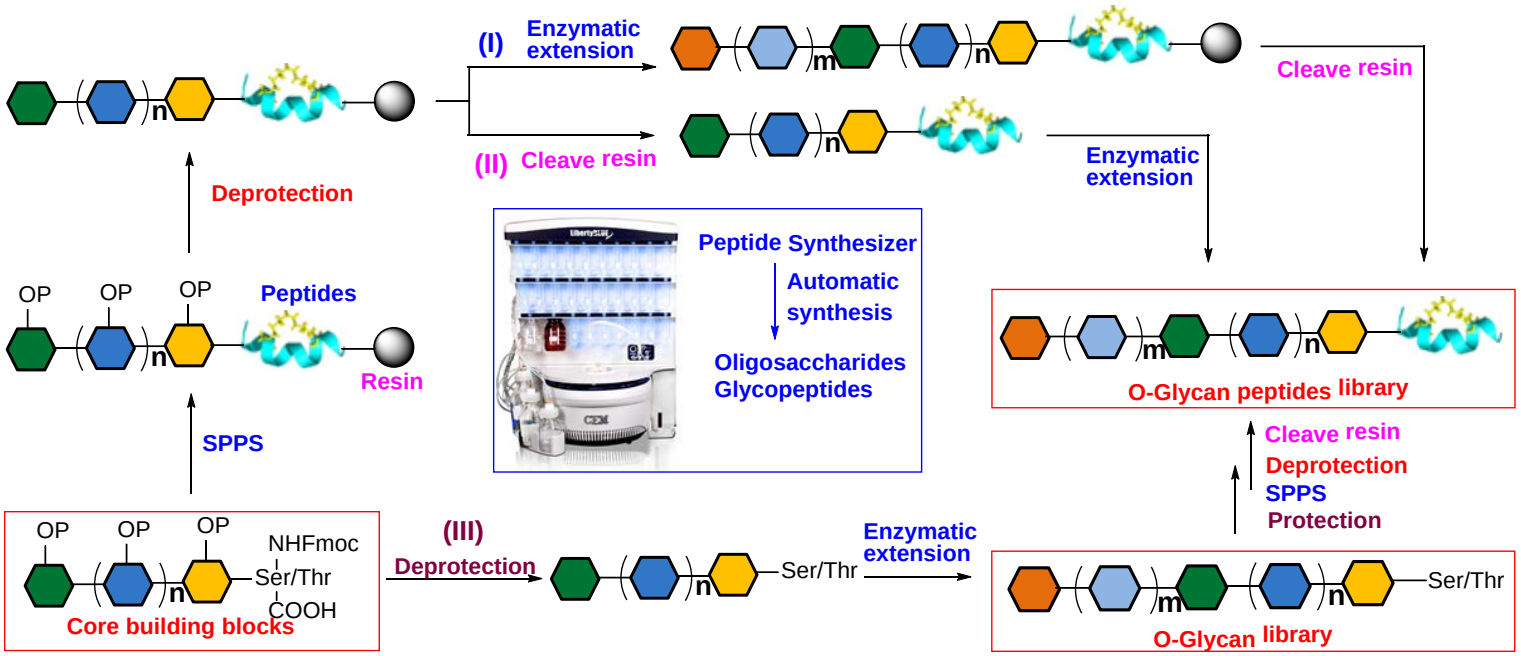
commonfund.nih.gov/Glycoscience

Matt Brichacek, University of Maine

umaine.edu/brichlab/

Facile Synthesis of O-glycans & O-glycopeptides

NIH Common Fund Glyco-science Program (U01GM116263)
Peng George Wang & Lei Li, Georgia State University

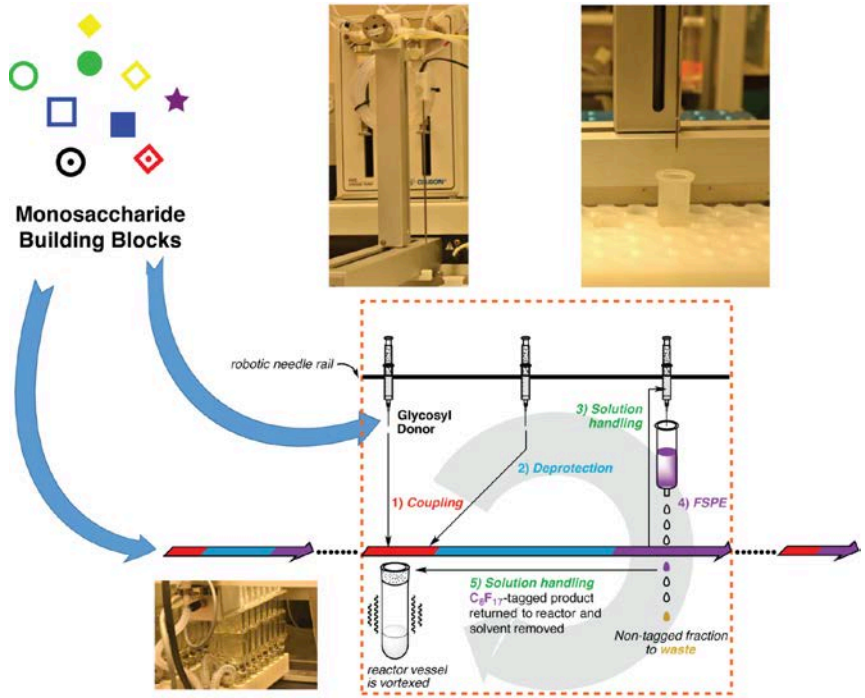


Goal: Develop “Core Synthesis/Enzymatic Extension” strategy for the access of O-glycan and O-glycopeptide librieres, automated glyopeptide synthesis

- Convergent chemical synthesis of O-glycan core structures in gram scale;
- Enzymatic extension strategy allows diversity of core structures;
- Automatic glycopeptide synthesis on solid phase/water soluable supports;
- Synthesis of hundreds of O-glycans and O-glycopeptides;
- Cross-validation

Common Fund Research in the Pohl/Dong Groups: Sugar Building Blocks and Automated Synthesis of Biomedically-Relevant Glycans

Developing Chemical Methods to Access Building Blocks and Create Oligosaccharides Using Solution-Phase Automation Platforms

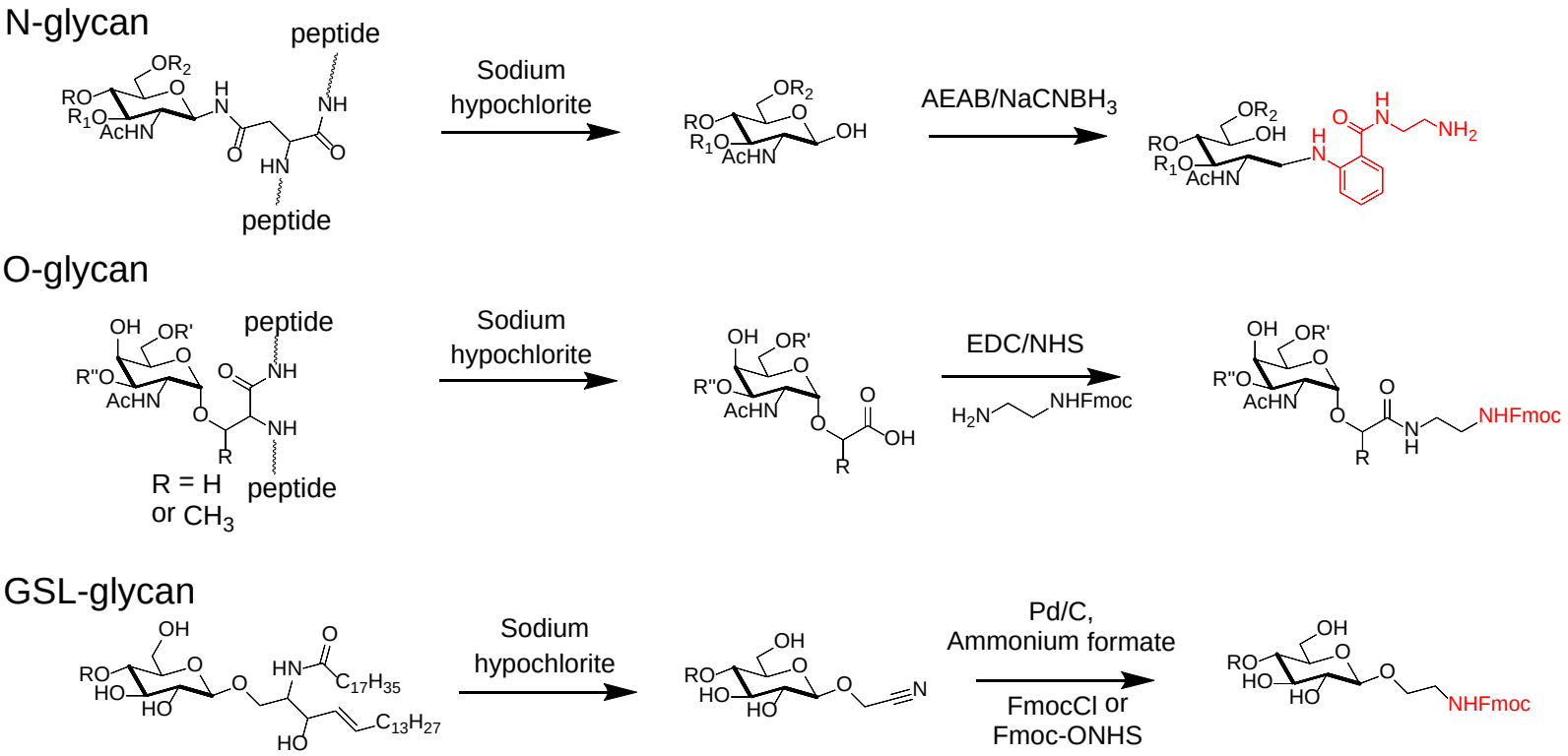


Human Milk Oligosaccharides, Bacterial Rhamnans, and Mammalian O- and N-Glycans

- ***Analytical standards and compounds for bioassays with the potential to incorporate fluorescent and other labels***
- ***New methods to purify synthetic glycans to 99.5%+ purity for immunological studies*** *(Chem Commun.* **2016**, *52*, 13253*)*

https://commonfund.nih.gov/Glycoscience/fundedresearch#

Large scale chemical preparation of glycans from natural sources



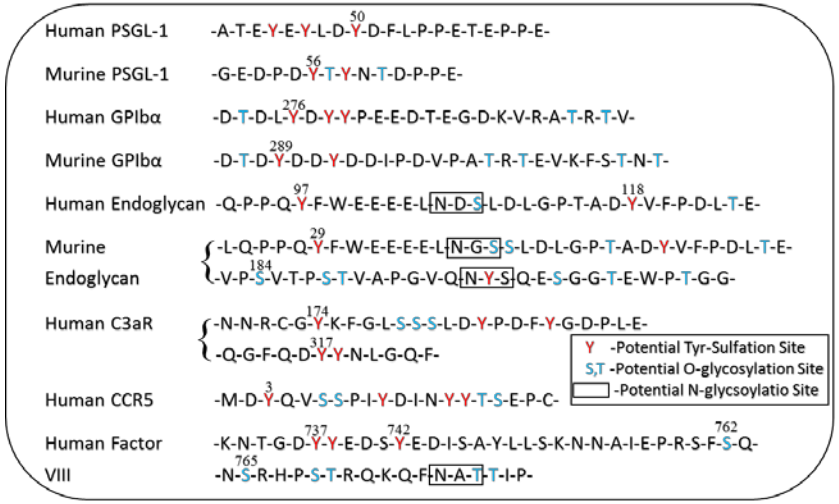
- Novel methods for large scale chemical release and multi-dimensional HPLC separation of natural glycans *Xuezheng Song, Emory University*
- Detailed structure characterization/confirmation of natural glycans *Vernon Reinhold, University of New Hampshire Glycomics Center*

U01GM116254 *Common Fund for Glycoscience*

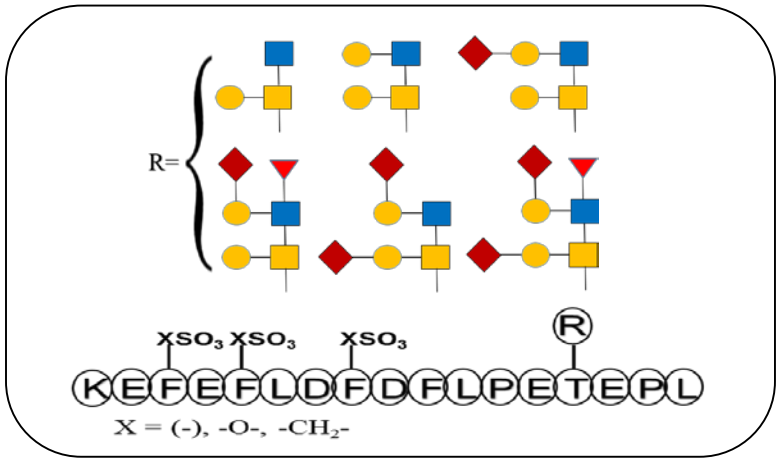
Chaikof Group

Facile Synthesis of Glycosulfopeptides (GSPs) and Related Bioconjugates

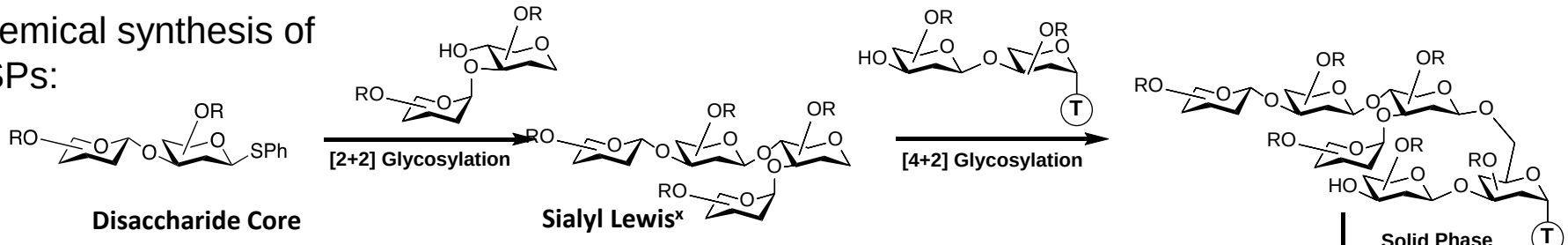
Nature's GSPs:



Our GSPs:



Chemical synthesis of GSPs:



- Scalable chemical synthesis of Sialyl Lewis^X
- Total synthesis of GSnP-6 and other glycosulfopeptides
- Next generation synthesis of Sialyl Lewis^X with acetyl protecting groups

Krishnamurthy, V. R.; Sardar, M. Y. R.; Ying, Y.; Song, X.; Haller, C.; Dai, E.; Wang, X.; Hanjaya-Putra, D.; Sun, L.; Morikis, V.; Simon, S. I.; Woods, R. J.; Cummings, R. D.; Chaikof, E. L. *Nat. Commun.* **2015**, *6*, 6387.

UO1GM116196