Research

RESEARCH INTERESTS

- Stereocontrol and other mechanistic aspects of chemical glycosylation. Novel glycosylation reactions.
- Regioselective protection of carbohydrate molecules. Design and application of modern protecting groups and strategies to the versatile synthesis of building blocks.
- Metal complexes in synthetic carbohydrate chemistry: direction of the stereoselectivity of glycosylation, regioselectivity, activation, temporary deactivation, switchable stereoselectivity, etc.
- Expeditious strategies for the synthesis of complex oligosaccharides and glycoconjugates: chemoselectivity and orthogonality of modern glycosyl donors.
- Solid phase and surface chemistry: application to stereoselective glycosylation and rapid assembly of complex oligosaccharides and glycoconjugates.
- Combinatorial and automated synthesis. New platforms and technologies for automated oligosaccharide synthesis: STICS and HPLC-based approaches.
- Fully synthetic glycopharmaceuticals based on carbohydrates with potential biological activity (anti-cancer, anti-inflammatory, antiseptic, antibacterial, etc.).
- Synthetic glycoproteins, glycopeptides, glycopolymers, glycolipids, glycoheterocycles, glycoaminoacids and combinations thereof. Synthetic glycoconjugate vaccines.
- Human milk oligosaccharides and other food additives and ingredients. Oligosaccharides as prebiotics.

CONTRIBUTIONS TO SCIENCE

With participation of more than 130 co-workers/trainees, my laboratory has developed many innovative tools for the synthesis and application of carbohydrates in the following major areas.

1. ***Development of new reagents, protecting groups, and building blocks.*** The application of partially protected building blocks is fundamental to carbohydrate chemistry. Poor accessibility to building blocks hampers the development of all synthetic methods and researchers experience significant setbacks because they must continue to remake building blocks. There are no universal building blocks, protecting groups, reagents or methods for the synthesis of glycans. My lab has been working on developing new protecting groups and advanced synthetic intermediates that will provide streamlined access to regioselectively protected building blocks. In recent years, we have also initiated a program dedicated to the development of new catalysts and protocols for catalytic activation and modification of carbohydrates. Articles describing new reagents, protecting groups, and building blocks. *Here and below the numbers correspond to the article number, as listed in the current cv. Interdisciplinary articles are cross-listed under different categories*: 31, 32, 34, 41, 42, 44, 45, 56, 57, 62, 65, 66, 68, 79, 101-103, 110, 125-127, 136, 137, 140, 151, 156, 161, 166, 170, 174, 178
2. ***Stereocontrolled glycosylation: reactions and mechanism.*** Many complex sugars have an oligomeric sequence wherein monosaccharides are linked via O-glycosidic linkages. This linkage is obtained by a glycosylation reaction which, despite significant progress, remains challenging due to the requirement to achieve complete stereocontrol and to suppress side reactions. To address these challenges, my lab introduced the thioimidate glycosylation approach, discovered the O-2/O-5 cooperative effect in glycosylation, and invented an ether-type participating group. My team developed many methods for 1,2-cis glycosylation including bromine-activated glycosidation of thioglycosides, H-bond mediated aglycone delivery, and a metal-coordination

approach to controlling stereoselectivity. Very recently, my lab invented the concept of regenerative glycosylation reactions. Articles describing new glycosylation reactions, stereocontrol, new leaving groups, and reaction mechanism: 2-5, 7, 9, 10, 12-14, 16-20, 22, 23, 25-27, 29, 30, 33, 38-40, 44, 48, 50-52, 55, 57, 60, 62, 76, 78, 79, 84, 87, 88, 91, 92, 100, 103, 105, 106, 110, 112, 113, 115, 119, 120, 122, 124, 125, 131, 133, 135, 137, 140, 142, 143, 149-152, 154, 158, 159, 164, 166, 167, 169, 171, 173, 177

3. ***Oligosaccharide synthesis: expeditious strategies and automated technologies.*** Glycosylation represents only one challenge oligosaccharide synthesis researchers face; often additional protecting or leaving group manipulations between each glycosylation step are required. This becomes increasingly inefficient at advanced stages of the assembly, often leading to a dramatic drop in yield, and, consequently, a decrease in the availability of oligosaccharides. To address these challenges, my lab introduced the following strategies for expeditious oligosaccharide synthesis: the temporary deactivation concept, the inverse armed-disarmed strategy, electronically superarmed and superdisarmed building blocks, templated oligosaccharide synthesis, and the reverse orthogonal strategy. My group also developed five new sets of leaving groups for orthogonal activation. More recently, my lab has been working on automated technologies for oligosaccharide synthesis: STICS (Surface-Tethered Iterative Carbohydrate Synthesis) and HPLC-assisted automated synthesis in collaboration with Keith Stine, a biophysical surface chemist in our Department. Articles describing oligosaccharide/ polysaccharide synthesis and modification: 1, 6, 8, 11, 15, 21, 24, 30, 35, 37, 39, 43, 44, 46, 47, 49, 50, 51, 54, 56, 59, 63, 64, 67, 68, 70-73, 77, 82, 88, 90, 91, 93, 96, 97, 105, 107, 113, 129, 138, 143-145, 148, 150, 151, 152, 156, 158, 163, 168; Articles describing new technologies for the automated glycan synthesis: 71, 107, 118, 139, 145, 163, 171, 172, 175

4. ***Biomedical studies: development of glycopharmaceuticals.*** The synthetic methods discussed in the previous sections have been applied to the synthesis of biologically important or therapeutically relevant molecules. Our lab synthesized and studied carbohydrate molecules to determine their involvement in biological processes associated with various human diseases. Recent collaborative projects include syntheses of tumor-associated glycosphingolipids that mediate the metastasis of carcinomas (with Stine) and those involved in pathogenesis of Krabbe disease (with Sands). My lab has obtained glycoconjugates of *S. pneumoniae*, serogroups 6 and 14 (with Nahm), as well as *Staph. aureus* types 5 and 8 (with Pfizer), important bacterial pathogens. My group has synthesized a series of glycopeptides as anti-septicemia (with Nichols) and anti-cancer therapeutics (with Spadaro). A series of our compounds have been investigated as imaging reagents *in vivo* (with Wang). We have also been studying thioimidates (with Byers and with Daniellou) and aminosugars (with Orlean and Price) as inhibitors or substrates for various enzymes. Articles describing development of vaccines, pharmaceuticals, and diagnostics: 15, 21, 28, 46, 54, 61, 64, 74, 77, 81, 89, 95, 99, 108, 111, 114, 116, 117, 121, 123, 128, 130, 132, 138, 141, 144, 146, 165, 168, 171, 172, 175, 176

5. ***Carbohydrate nanotechnology: integration of glycans and nanomaterials.*** My lab synthesized and studied carbohydrate molecules to determine their utility in biosensing and electroanalytical applications. In collaboration with Professor Keith Stine (UMSL) we studied the application of porous nanostructured materials to the supported synthesis of glycans. We have also investigated the application of porous nanomaterials to detecting carbohydrate-protein interactions by electrochemical and spectroscopic means. Other applications of nanoporous gold material include separation, enrichment, and biosensing of glycoproteins. Articles describing integration of glycans and nanomaterials: 53, 61, 71, 94, 104, 108, 114, 116, 123, 132, 134, 141, 146, 147, 153, 155, 157, 160, 162, 165

6. ***Other projects.*** My laboratory has been involved in several other collaborative and individual projects that span across a few research areas. These projects are listed below, and representative citations are given. Articles describing metal complexes with carbohydrates: 34, 35, 67, 76, 83, 140, 142. Articles describing thermochemical and theoretical studies: 58, 75, 80, 86, 98, 174