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Education

- Postdoctoral fellow, Section of Leukocyte Biology, Dept. of Pediatrics, 1995-1997
Baylor College of Medicine, Houston, TX
Research topic: "Neutrophil cell adhesion dynamics under fluid shear" (Mentors: Scott I. Simon, C. Wayne Smith)
- Ph.D., Bioengineering/Chemical Engineering, May 1996
Rice University, Houston, TX.
Dissertation title: "Mechanisms of homotypic lymphocyte aggregation and cell motility induced by activation of VLA integrins" (Advisor: Kyriacos Zygourakis)
- B.Tech., Chemical Engineering, July 1991
Indian Institute of Technology, Delhi, India

Positions and Honors

Positions and Employment

1991-1995 Research Assistant, Chemical Engineering Department, Rice University, Houston, TX
1995-1997 Research Associate, Pediatrics Department, Baylor College of Medicine, Houston, TX
1997-2003 Assistant Professor, Chemical Engineering Department, SUNY Buffalo, Buffalo, NY
2002-present Co-director, Center for Biomedical Engineering, SUNY Buffalo, Buffalo, NY
2003-2008 Associate Professor, Chemical and Biological Engineering, SUNY Buffalo, Buffalo, NY
2006-present Member, NY State Center for Excellence in Bioinformatics and Life Sciences, Buffalo, NY
2007-2008 Director of Graduate Studies, Chemical and Biological Engineering, SUNY, Buffalo, NY
2008-present Professor, Dept. of Chemical and Biological Engineering, SUNY Buffalo, Buffalo, NY
2008-present Professor, Dept. of Chemical and Biological Engineering, SUNY Buffalo, Buffalo, NY
2016-present Faculty, UB Clinical Translational Research Center, Buffalo, NY
2017-present Research Professor, Dept. of Medicine, Jacobs School of Medicine and Biomedical Sciences, SUNY, Buffalo, NY

Honors and Selected Professional Activities

1991 -1992 Rice University Fellowship
1995 Graduate Student Symposium Winner, Rice University
1996 Sigma Xi Scientific Research Society Dissertation Recognition
1999 Reifler Award, State University of New York at Buffalo
2001 1 of 100 Members of the Upstate Alliance of Innovators, Western New York
2002 Exceptional Scholar Program: Young Investigator Award, SUNY at Buffalo
2003-2015 Honoree, Science, Technology Transfer and Economic Outreach (STOR) Office and The SUNY Research Foundation on three occasions (for issued and licensed patents)
2004 Independent Scientist Award, National Heart, Lung and Blood Institute, NIH
2009-2012 Full member, NIH standing study section on Hypertension and Microcirculation
2010, 2014 Invited speaker, Annual meeting of the Society of Glycobiology
2011 Exceptional Scholar Program: Sustained Achievement Award, University at Buffalo
2012 Elected Fellow, American Institute for Medicine and Biological Engineering
2015 SUNY Chancellor's Award for Excellence in Scholarship and Creative Activities
2017-present Discussion leader, Symbol Nomenclature for glycans (SNFG) & Member, Glycan Informatics Advisor group at NCBI-Glycans (<https://www.ncbi.nlm.nih.gov/glycans/>)

Editorial Service: Associate Editor, *Annals of Biomedical Engineering*, 2009-present; Associate Editor, *Frontiers in Computational Physiology and Medicine* (2011-present); Associate Editor, *Frontiers in Biomechanics* (2013-present); Editorial Board Member, *Cell Communication and Adhesion*, 2001-2006; Guest Editor for special Issue of *Annals of Biomedical Engineering*, 2008; Editorial Board, *Journal of Glycomics & Lipidomics*, 2010-present.

Grant Reviewer: NIH Ad Hoc Reviewer for various panels related to: Bioengineering Research Partnership (2005-2006), NHLBI Systems Biology (2006-2007, 2012-2015); Microcirculation and Hypertension (2007-2009, regular member 2009-2012); ZRG1 HM (02) (2011); ZRG1 CVRS-F (02) (2011); ZRG1 IDM-V-02 (2013); ZRG1 VH-D (50) (2013); ZRG1 VH-D (50) (2013); ZRG1 VH-D (55) (2014); ZRG1 VH-D (55) (2014); ZRG1 VH-D55 (2015); BST-U(50) (2015); Thrombosis and Hemostasis (HT, 2015, 2017, 2018); ZRG1 MOSS-Q(02) (2017); ZRG VH-B (03) (2017); ZAI1 PA-I (J1) (2017), ZRG1 BST-H(40) (2018), Also panel member for National Science Foundation, and also various funding agencies in Europe, Australia and Asia.

Professional Memberships: American Institute of Chemical Engineers (AIChE), Biomedical Engineering Society (BMES), ASBMB, Federation of American Societies of Experimental Biology (FASEB), American Association for the Advancement of Science (AAAS), International Society of Thrombosis and Haemostasis (ISTH), Society of Glycobiology (SFG)

Contributions to BMES: Member since 1996; BMES Affiliations committee member (2009-10); Associate Editor, *Annals of Biomedical Engineering*, 2009-present; Reviewer and session chair at various BMES annual meetings (2010-2018).

Research interests summary:

Systems Glycobiology: We are interested in studying mammalian glycosylation pathways, particularly with respect to developing systems biology tools. Here, we develop mathematical models of cellular glycosylation with the goal of providing a platform that will integrate experimental data being collected at the transcript and protein level with biochemical reaction pathways and glycan structures (open source software available at VirtualGlycome.org). Experimental validation of these models is performed using large scale experiments (Next Generation Sequencing/NGS and high-throughput tandem mass spectrometry/MS), protein engineering and biochemical methods. Additional testing is conducted using systems perturbation approaches by applying small molecule inhibitors and genome editing (CRISPR) tools. In particular, we are interested in a family of ~200 enzymes called glycosyltransferases that constitute 1% of the human genome, and the competition between them which regulates the site-specific pattern of glycosylation on a variety of cell surface glycoproteins and glycolipids. This fundamental understanding is critical for developing a broad range of early detection biomarkers and therapeutic strategies for cardiovascular, inflammatory and cancer-related disorders.

Thrombosis and Hemostasis: The goal of this project is to develop novel methods to control coagulation in blood, and to define novel technologies to control the balance between clotting and bleeding. In particular, the focus is on Von Willebrand factor structure-function studies, protein biophysics and self-association function, and arterial and microvascular mouse models of thrombosis. These studies examine the effect of physiological and pathological hydrodynamic shear on a variety of biological/clotting phenomena that occur in human blood.

Inflammation biology: The studies analyze the basic biological processes regulating human leukocyte adhesion with vascular endothelial cells that line the blood vessels. Besides identifying the roles of glycans, carbohydrate binding lectins and integrins in this multi-step cell adhesion cascade, a major effort of this project also focusses on metabolic strategies to perturb leukocyte O- and N-linked glycans. To this end, a series of chemical monosaccharide and substrate analogs have been developed that when fed to the white blood cells, these entities fine tune or modify their interaction

with the vessels walls in mouse models of acute inflammation and chronic obstructive pulmonary disorder. This project thus aims to develop anti-inflammatory drugs using small molecules to perturb selected carbohydrate biosynthesis metabolic pathways.

Regenerative medicine: The goal of this project is to develop cell adhesion engineering/CAE strategies to target stem cells and stem cell derived exosomes to the heart in models of myocardial infarction. To this end, we perform the glycan engineering of mesenchymal stem cells (MSCs), cardiosphere-derived cells (CDCs) and cardiac stem cells (CSCs). Methods to improve the targeting of these modified stem cells to ischemic sites are developed in a large-animal swine model. Advanced imaging methods are also developed as part of this project to monitor and optimize the targeted delivery of stem cell therapeutics.

Bibliography

Publications: Open source software

We maintain three software related to Systems Glycobiology at our web server: www.VirtualGlycome.org. These have each been downloaded several 100-times by members of the scientific community.

S1. DrawGlycan-SNFG: Used for sketching/rendering glycans using IUPAC condensed input strings. This program is directly linked to NCBI pages related to glycans.

Availability: <https://virtualglycome.org/drawglycan/>; <http://drawglycan.sourceforge.net/>; <https://github.com/kaichengub/DrawGlycan-SNFG>

S2. GlycoProteomics Analysis Toolbox (GlycoPAT): Program for high-throughput glycoproteomics mass spectrometry data analysis using tandem-MS data.

Availability: <https://virtualglycome.org/glycopat/>; <http://glycopat.sourceforge.net/>; <https://github.com/kaichengub/GlycoPAT>

S3. Glycosylation Network Analysis Toolbox (GNAT): Generating carbohydrate biosynthesis reaction networks from mass spectrometry and transcriptomics data interpretation.

Availability: <https://virtualglycome.org/gnat/>; <http://gnatmatlab.sourceforge.net>

Publications: Full-length Refereed Journal Articles

- J1. Wang, S.S., Gao, X., del Solar, V., Yu, X., Antonopoulos, A., Friedman, A.E., Matich, E. K., Atilla-Gokcumen, G.E., Nasirikenari, M., Lau, J.T., Dell, A., Haslam, S. M., Laine, R.A., Matta, K.L. and Neelamegham, S. Thioglycosides are efficient metabolic decoys of glycosylation: Reduction of selectin dependent leukocyte adhesion, *Cell Chemical Biology* (pending revision, 2018).
- J2. Chugh, S., Barkeer, S., Rachagani, S., Nimmakayala, R.K., Pothuraju, R., Atri, P., Thapa, I., Sheinin, Y.M., Talmon, G.A., Smith, L.M., Yu, X., Neelamegham, S., Xia, L., Ponnusamy, M.P., Batra, S.K., "Genetic Deletion of Core 1 β 1, 3-galactosyltransferase Leads to Early Onset and Metastasis of Pancreatic Adenocarcinoma", *Gastroenterology*, in press, 2018.
- J3. Ferguson, S.W., Wang, J., Lee, C.J., Lu, M., Neelamegham, S., Canty, J.M., Nguyen, J. The microRNA regulatory landscape of MSC-derived exosomes: a systems view. *Scientific Reports*. 2018 Jan 23;8(1):1419. doi: 10.1038/s41598-018-19581-x.
- J4. Zhang, C., Kelkar, A., Nasirikenari, M., Lau, J.T.Y., Sveinsson, M., Sharma, U.C., Pokharel, S., Neelamegham, S. The physical spacing between the VWF D'D3- and A1- domains regulates platelet adhesion in vitro and in vivo *J Thromb Haemost*. 16(3):571-82. 2018. doi: 10.1111/jth.13927
- J5. Gogia, S., Kelkar, A., Zhang, C., Dayananda, K. M., Neelamegham, S., Role of calcium in regulating the intra- and extra-cellular cleavage of von Willebrand factor by the protease ADAMTS13. *Blood Advances* 2017 Oct 20;1(23):2063-2074. doi: 10.1182/bloodadvances.2017009027

- J6. Liu, G., Cheng, K., Lo, C. Y., Li, J., Qu, J., Neelamegham, S., A comprehensive, open-source platform for mass spectrometry based glycoproteomics data analysis *Molecular and Cellular Proteomics* 2017 Nov;16(11):2032-2047. doi: 10.1074/mcp.M117.068239.
- J7. Zhang C, Neelamegham S. Application of microfluidic devices in studies of thrombosis and hemostasis *Platelets*. 2017 Jul; 28(5):434-440.
- J8. Cheng K, Zhou Y, Neelamegham S DrawGlycan-SNFG: a robust tool to render glycans and glycopeptides with fragmentation information *Glycobiology*. 2017 Mar 15;27(3):200-205.
- J9. Chitgupi U, Li Y, Chen M, Shao S, Beitelshes M, Tan MJ, Neelamegham S, Pfeifer BA, Jones C, Lovell JF. Bimodal Targeting Using Sulfonated, Mannosylated PEI for Combined Gene Delivery and Photodynamic Therapy *Photochem Photobiol*. 2017 Mar;93(2):600-608.
- J10. Buffone A Jr, Nasirikenari M, Manhardt CT, Lugade A, Bogner PN, Sackstein R, Thanavala Y, Neelamegham S, Lau JT Leukocyte-borne $\alpha(1,3)$ -fucose is a negative regulator of $\beta 2$ -integrin-dependent recruitment in lung inflammation. *J Leukoc Biol*. 2017 Feb;101(2):459-470
- J11. Momeni A, Neelamegham S, Parashurama N. Current challenges for the targeted delivery and molecular imaging of stem cells in animal models. *Bioengineered*. 2016 Nov 4:1-9.
- J12. Neelamegham S, Mahal LK. Multi-level regulation of cellular glycosylation: from genes to transcript to enzyme to structure. *Curr Opin Struct Biol*. 2016 Oct;40:145-152.
- J13. Stolfa G, Mondal N, Zhu Y, Yu X, Buffone A Jr, Neelamegham S. Using CRISPR-Cas9 to quantify the contributions of O-glycans, N-glycans and Glycosphingolipids to human leukocyte-endothelium adhesion. *Scientific Reports*. 2016 Jul 26;6:30392.
- J14. Chandrasekaran EV, Xue J, Xia J, Khaja SD, Piskorz CF, Locke RD, Neelamegham S, Matta KL Novel interactions of complex carbohydrates with peanut (PNA), Ricinus communis (RCA-I), Sambucus nigra (SNA-I) and wheat germ (WGA) agglutinins as revealed by the binding specificities of these lectins towards mucin core-2 O-linked and N-linked glycans and related structures. *Glycoconj J*. 2016 Oct;33(5):819-36.
- J15. Nascimbene A, Neelamegham S, Frazier OH, Moake JL, Dong JF. Acquired von Willebrand syndrome associated with left ventricular assist device. *Blood*. 2016 Jun 23;127(25):3133-41.
- J16. Mondal N, Stolfa G, Antonopoulos A, Zhu Y, Wang SS, Buffone A Jr, Atilla-Gokcumen GE, Haslam SM, Dell A, Neelamegham S. Glycosphingolipids on Human Myeloid Cells Stabilize E-Selectin-Dependent Rolling in the Multistep Leukocyte Adhesion Cascade *Arterioscler Thromb Vasc Biol*. 2016 Apr;36(4):718-27.
- J17. Gupta R, Matta KL, Neelamegham S. A systematic analysis of acceptor specificity and reaction kinetics of five human $\alpha(2,3)$ sialyltransferases: Product inhibition studies illustrate reaction mechanism for ST3Gal-I *Biochem Biophys Res Commun*. 2016 Jan 15;469(3):606-12.
- J18. Lo CY, Weil BR, Palka BA, Momeni A, Canty JM Jr, Neelamegham S. Cell surface glycoengineering improves selectin-mediated adhesion of mesenchymal stem cells (MSCs) and cardiosphere-derived cells (CDCs): Pilot validation in porcine ischemia-reperfusion model. *Biomaterials*. 2016 Jan;74:19-30.
- J19. Gogia S, Neelamegham S. Role of fluid shear stress in regulating VWF structure, function and related blood disorders. *Biorheology*. 2015;52(5-6):319-35. doi: 10.3233/BIR-15061.
- J20. Chitgupi U, Zhang Y, Lo CY, Shao S, Song W, Geng J, Neelamegham S, Lovell JF. Sulfonated Polyethylenimine for Photosensitizer Conjugation and Targeting. *Bioconjug Chem*. 2015 Aug 19;26(8):1633-9. doi: 10.1021/acs.bioconjchem.5b00241.
- J21. Gogia, S., Lo, C.Y., Neelamegham, S., Detection of plasma protease activity using microsphere-cytometry assays with *E. coli* derived substrates: VWF proteolysis by ADAMTS13 *PLoS One*. 2015 May 18;10(5):e0126556.
- J22. Liu, G., Neelamegham, S. "Integration of systems glycobiology with bioinformatics toolboxes, glycoinformatics resources, and glycoproteomics data." *Wiley Interdiscip Rev Syst Biol Med*. 2015 Jul-Aug;7(4):163-81. doi: 10.1002/wsbm.1296.

- J23. Hubbard AR, Heath AB, Kremer Hovinga JA; Subcommittee on von Willebrand Factor. Establishment of the WHO 1st International Standard ADAMTS13, plasma (12/252): communication from the SSC of the ISTH *J Thromb Haemost.* 2015 Jun;13(6):1151-3
- J24. Shao, S., Geng, J., Yi, H-A., Gogia, S., Neelamegham, S., Jacobs, A., Lovell, J.F. "Polyhistidine-Tagged Ligand and Antigen Binding to Cobalt Porphyrin Bilayers", *Nat Chem.* 7(5):438-46, 2015.
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- J30. Mondal, N., Buffone, A., Neelamegham, S. "Distinct glycosyltransferases synthesize E-selectin ligands in human vs. mouse leukocytes", *Cell Adhesion and Migration.* 7(3):288-92, 2013.
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- J38. Chandrasekaran E.V., Xue J., Xia J., Locke R.D., Patil S.A., Neelamegham S., Matta K.L. "Characterization of cancer associated mucin type O-glycans using the exchange sialylation properties of mammalian sialyltransferase ST3Gal-II", *J Proteome Res.* 11(4):2609-18, 2012.
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- J42. Barthel, S.R., Antonopoulos, A., Cedeno-Laurent, F., Schaffer, L., Hernandez, G., Patil, S.A., North, S.J., Dell, A., Matta, K.L., Neelamegham, S., Haslam, S.M., Dimitroff, C.J. "Peracetylated 4-fluoro-glucosamine reduces the content and repertoire of N- and O-glycans without direct incorporation", *J. Biol. Chem.*, 286(24):21717-31, 2011.
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- J44. Dayananda, K. M., Gogia, S., Neelamegham, S. "E. coli derived Von Willebrand Factor-A2 domain FRET proteins that quantify ADAMTS13 activity", *Analytical Biochemistry*, 410(2):206-13, 2011.
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- J47. Marathe, D.D., Buffone Jr. A., Chandrasekaran E.V., Nasirikenari, M., Lau, J.T.Y., Matta, K.L., Neelamegham, S. "Fluorinated GalNAc metabolically alters glycan structures on leukocyte PSGL-1 and reduces cell binding to selectins" 115(6):1303-12, *Blood*, 2010. [Editorial on this article published by Nature-Consortium for Functional Glycomics]
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Publications: Book Chapters

- B1. Madabhushi, S. and Neelamegham, S., "Mechanisms of Platelet Activation by Biomaterials and Fluid Shear flow", *Biomaterials Science: Processing, Properties and Applications III: Ceramic Transactions*, Volume 242, pg. 113-123, 2013.
- B2. Beauharnois, M.B., Neelamegham, S. and Matta, K.L., "Quantitative measurement of selectin-ligand interactions: Assays to identify a sweet pill in a library of carbohydrates", *Glycobiology Protocols- Methods Mol Biol*, pg. 343-358, 2006.
- B3. Zhang, Y. and Neelamegham, S., "Blood Cell counter", Second Ed. *Wiley Encyclopedia for Biomedical Instrumentation*, pg. 81-90, 2006.
- B4. Neelamegham, S. and Matta, K.L., "Liposomes containing ligands: Binding Specificity to selectins", *Methods in Molecular Biology: Liposome Methods and Protocols*, Humana Press, New York, 199:175-91. 2002.

Publications: Patents

- P1. "Fluorescence resonance energy transfer (FRET) based measurement of ADAMTS-13 activity", Neelamegham, S., Dayananda, K. M., US provisional patent 61/351318 (2010), Non-provisional US patent Application No. 13/701,930.
- P2. "Methods for Synthesis of Sialylated products using reversible sialylation", Matta, K.L., Chandrasekaran, E.V., Neelamegham, S., Xue, J. US patent 8,278,072 (2012).
- P3. "Extraction of liquid from absorbent packaging", Alexandridis, P., and Neelamegham, S., U.S. patent 6,589,797 (2003) [licensed to Technicor, Inc., Buffalo, NY].
- P4. "Extraction of liquid from absorbent packaging", Alexandridis, P., and Neelamegham, S., U.S. patent 7,008,797 (2006) [licensed to Technicor, Inc., Buffalo, NY].
- P5. "Functional antibodies that recognize the D'D3 domain of human VWF", Neelamegham, S., S. R. Madhabushi, K. Rittenhouse Olson, US Provisional patent, July 20, 2011.
- P6. "Metabolic inhibitor of selectin mediated cell adhesion" Neelamegham, S. Marathe, D.D., Buffone, A., Lau, J.T. Matta, K.L., US provisional patent 61/102,600 (2008).
- P7. "Novel family of selectin antagonists", S. Neelamegham and K. Matta, U.S. patent 60/670,163

Selected invited seminars and lectures (2018 only)

1. S. Neelamegham, "Analysis of high-throughput glycoproteomics mass spectrometry experiments" 29th International Carbohydrate Symposium, Lisbon, Portugal, 2018.
2. "Role of glycans in regulating leukocyte adhesion biomechanics and cellular signaling", World Congress of Biomechanics, Dublin, Ireland, 2018.
3. "Glycan structures regulating human inflammatory diseases", Department of Biomedical Engineering, University of California- Davis, 2018.
4. S. Neelamegham, "Systems level analysis of glycosylation—new tools to profile the metabolome", Department of Biomedical Engineering, Rutgers University, NJ, 2018.
5. S. Neelamegham, "Glycoinformatics tools to analyze and curate large scale experimental datasets", International Life Science Integration Workshop, Tokyo, Japan, 2018.
6. S. Neelamegham, "New developments at *VirtualGlycome.org*", Society for Glycobiology-Glycoinformatics satellite, Portland, OR, 2017.

Research Support (current)

R01HL103411 (Neelamegham) 09/05/2011 – 05/31/2021

National Institutes of Health

"Systems Biology of Glycosylation"

Goals: This RO1 develops mathematical modeling methods and complementary experiments to study cellular glycosylation reaction networks. The idea is to develop a framework for mathematical modeling of glycosylation processes, to develop hypotheses *in vitro* using human blood and to test them in studies of chronic inflammation to study end effector cell function.

Role: PI

1R21GM126537-01 (Neelamegham) 12/15/2017-11/30/2019

National Institutes of Health

“Synthetic glycan biomarkers: Novel reporters of cell metabolism”

Goal: To develop a technology called ‘synthetic glycan biomarkers’ that will enable the longitudinal tracking of metabolic changes in live animal blood and urine samples

Role PI

161RG27770071 Neelamegham (PI) 1/1/2016 – 12/31/2018

American Heart Association

“Targeting cellular therapeutics in a pre-clinical model of myocardial infarction”

Goals: High-risk, high-reward pilot study grant supported through the AHA ‘Innovative Research Grant’ mechanism. The overall goal is to determine if stem cells engineered to have altered cell adhesion properties display enhanced homing and therapeutic efficacy in a myocardial infarction swine model.

Role: PI

1U01CA221229-01(Mahal) 7/1/2017-6/30/2020

National Institutes of Health

“GlycoMiR: Mapping the miRNA-glycogene interactome”

Goals: To map microRNA:glycogene interactions and create GlycoMiR, a database of MicroRNA:glycogene interactions.

Role: co-Investigator

P01HL107146 Sackstein/Lau (PI) 07/1/2011-05/31/2018

National Institutes of Health

“Regulation of Lactosaminyl Glycan Biosynthesis in Hematopoietic Cells”

Goals: This is a multi-investigator PO1 grant submitted from the Harvard Medical School in response to the Program of Excellence in Glycosciences RFA (HL-10-026). Here, as part of Aim 5 of project 2, I develop mathematical analysis methods to support the experimental work performed by Dr. Joseph Lau (Roswell Park Research Institute) in Aim 1-4 of project 2. The lead PI for the entire grant application is Dr. Robert Sackstein, Harvard.

Role: co-I on Project 2

Supervision of research

Current members:

Research Scientist:

1. Dr. Anju Kelkar (2013 - present): Develop novel biomolecular methods

Post-doctoral fellow:

2. Dr. Virginia del Solar (2016-present): Glycan chemistry and mass spectrometry

Ph.D. students:

3. Changjie Zhang (Ph.D. candidate, 2012-2018): “Fluid shear and von Willebrand Factor”
4. Kai Cheng (Ph.D. candidate, 2013-present): “Glycoproteomic tool development”
5. Yusen Zhou (Ph.D. candidate, 2013-present): “Multilevel regulation of glycosylation”
6. Yuqi Zhu (Ph.D. candidate, 2013-present): “Systems Glycobiology: Library based technologies”
7. Arezoo Momeni (Ph.D. candidate, 2014-present): “Glycan engineering of stem cells”
8. Xinheng Yu (Ph.D. candidate, 2015-present): “Synthetic Glycan Biomarkers”
9. Theodore Groth (Ph.D. candidate, 2017-present): “Mapping glycosylation pathways using massive data sets”
10. Gabrielle Pawlowski (Ph.D. candidate, 2017-present): “De novo algorithms for Glycome and Glycoproteome profiling”

Previous members: 8 post-docs; 15 Ph.D. and 8 M.S. students