

Joshua S. Sharp, Ph.D.
Curriculum Vitae

Associate Professor of Pharmacology
Department of BioMolecular Sciences
Associate Professor of Chemistry and
Biochemistry
Research Associate Professor
Research Institute of Pharmaceutical
Sciences

The University of Mississippi
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Education

Institution	Degree	Year
Oak Ridge National Laboratory and the University of Tennessee Graduate School of Genome Science and Technology Knoxville, Tennessee 37996 Dissertation Advisor: Dr. Robert L. Hettich; Dissertation entitled "Development of Hydroxyl Free Radical Chemistry for the Surface Mapping of Proteins" The University of Tennessee Department of Microbiology Knoxville, Tennessee 37996	Ph.D. Life Sciences, emphasis in Genome Science and Technology B.S. Microbiology <i>Cum laude</i>	2003 1999

Postdoctoral Training

Institution	Position	Dates
Laboratory of Structural Biology, National Institute of Environmental Health Sciences, National Institutes of Health Research Triangle Park, North Carolina 27709	Intramural Research Training Award (IRTA) Fellow	Nov. 2003 – April 2007

Employment

July 2019 – present: Associate Professor of Pharmacology, Department of BioMolecular Sciences, University of Mississippi. As an Associate Professor, my responsibilities include:

- Instruction in undergraduate, professional and graduate programs within the School of Pharmacy focusing on biochemistry, protein and carbohydrate chemistry, and organic and biological mass spectrometry, including:
 - PHCL 343 – Biochemical Foundations of Therapeutics
 - PHCL 541 – Problems in Pharmacology (Analysis of Glycosaminoglycans)

- PHCL 669 – Physiological Chemistry
- BMS 725 – Mass Spectrometry: Fundamentals and Applications
- May 15, 2020 – present: Director and Principle Investigator, Glycoscience Center of Research Excellence (GlyCORE), and NIH-funded P41 center focusing on the development of infrastructure and faculty expertise in glycoscience at the University of Mississippi
- August 2019 – present: Associate Professor of Chemistry and Biochemistry, University of Mississippi
- Establishment and leadership of an independent research group focusing on the development and application of novel mass spectrometry-based techniques for the analysis of protein three dimensional structure, protein-protein complexes, and protein-ligand binding interfaces; glycosaminoglycan analysis and sequencing; and determination of glycosaminoglycan structures of potential biomedical and pharmacological interest
- Formal mentorship of four postdoctoral trainees, eight graduate students, and ten undergraduate research assistants since 2015
- Mentorship of junior faculty in the department
- Participation in collaborative projects and grants within the department, the University of Mississippi, and other institutions worldwide
- Service to the department, the University of Mississippi, and the broader community.

2017 – present: Chief Technology Officer of GenNext Technologies, Inc. My responsibilities include directing the scientific program of GenNext Technologies as they seek to commercialize new solutions in protein photochemistry and protein pharmaceutical analysis; provide scientific and grantsmanship leadership in SBIR and STTR applications; advise our engineering team in the implementation of integrated solutions for photochemistry; and advise customers on experimental design, data collection and analysis for biotherapeutic higher order structure analysis.

2015 – June 2019: Assistant Professor of Pharmacology, Department of BioMolecular Sciences, University of Mississippi.

July 2019 – present: Research Associate Professor, Research Institute of Pharmaceutical Sciences

2015 – June 2019: Research Assistant Professor, Research Institute of Pharmaceutical Sciences

2019 – present: Adjunct Associate Professor, Department of Chemistry, The University of Georgia. As Adjunct Associate Professor, my duties include serving on and chairing graduate student committees directing and evaluating the progress of Ph.D. and Masters degree students in the Department of Chemistry.

2015 – 2019: Adjunct Assistant Professor, Department of Chemistry, The University of Georgia

2012 – 2017: Founding Partner and Chief Executive Officer of Photochem Technologies, LLC. This start-up business was developed to design and market structural biology solutions based on new technologies for the protein pharmaceutical industry. Responsible for the development of the core technology behind the company, direction of the scientific output, contact with potential clients and strategic partners, and the overall strategic direction of the start-up company.

2013 – 2015: Associate Research Scientist at the Complex Carbohydrate Research Center of the University of Georgia, Faculty of the University of Georgia Graduate School. As a Research Faculty member, developed and maintained an independent research group focusing on the development and application of novel mass spectrometry-based techniques for the analysis of protein three-dimensional structure, protein-protein and protein-ligand binding, and the determination of glycosaminoglycan sequences of biomedical and pharmaceutical interest. Secured NIH funding to advance my research program, both independently as Principal Investigator on an R01 grant, and as part of integrated interdisciplinary teams as a Co-Investigator on of a P41 grant and an SBIR grant. Directed the training and education of M.S. and Ph.D. students in the Department of Chemistry. Directed research training of undergraduate students in Chemistry. Provided collaborative support to various research efforts within the Complex Carbohydrate Research Center, the wider University of Georgia, and in the external academic and business communities. Taught segments in undergraduate and graduate coursework on Physical Biochemistry (BCMB 4110/6110 and CHEM 4110), Advanced Proteomics (BCMB 9300), Mass Spectrometry (CHEM 8810), Advanced Physical Biochemistry (BCMB 8040), and external CCRC training coursework on characterization of complex glycans by chromatography and mass spectrometry. Disseminated results of research through lectures and presentations to various departments and organizations, both within the University of Georgia system and in the broader scientific community. Served as peer reviewer for various journals and funding agencies, both nationally and internationally. Served as organizer and chair for meetings and workshops in the scientific community.

2009 – 2015: Adjunct Research Scientist, Department of Chemistry, University of Georgia.

2009 – present: Faculty Member, Graduate School of the University of Georgia

2007 – 2013: Assistant Research Scientist at the Complex Carbohydrate Research Center at the University of Georgia.

2003 – 2007: Intramural Research Training Award (IRTA) fellow with Dr. Kenneth Tomer in the Laboratory of Structural Biology, National Institute of Environmental Health Sciences, National Institutes of Health. Developed and applied novel methods for the structural analysis of oxidative damage-induced conformational change. Independently developed and applied methods for the quantitative and qualitative structural analysis of proteins and large protein complexes by narrow- and broad-range

specificity surface modification and mass spectrometry. Developed and pursued research in peptide-hydroxyl radical chemistry. Developed and applied methods for determining structure of gas-phase rearrangement ions by formation of solution-phase analogs and MSⁿ. Directly mentored an undergraduate student researcher in research leading to a publication. Provided analytical and protein chemistry expertise in various collaborative projects examining protein structure and protein-protein interactions. Independently wrote and submitted NIH grant applications under the K22 and K99/R00 funding mechanisms.

2001 – 2003: Graduate research assistant for Dr. Robert Hettich at Oak Ridge National Laboratory and Dr. Jeffrey Becker at the University of Tennessee. Developed a method for the analysis of protein structure in solution by peroxide-mediated hydroxyl radical protein footprinting surface modification and mass spectrometry; collaborated with computational biologists and an X-ray crystallography lab to use surface modification data to model structures of novel proteins. Supervised the work of two junior graduate students and an undergraduate student on research I initiated. Assisted in securing independent funding for the project I initiated from the Department of Energy. Assisted in the preparation of an R01 NIH grant based on my graduate research, which was funded in 2004. Assisted in the teaching of a biological mass spectrometry survey course.

2000 – 2001: Teaching assistant for the Genome Science and Technology Program at the University of Tennessee, Knoxville. Assisted in instruction of an upper-level undergraduate biochemistry course for majors and a graduate survey course in bioinformatics and analytical biochemistry. Responsible for student discussion sessions, course web sites, demonstrations, student evaluation, course evaluation, and some lectures.

1999: Graduate Fellow in the Biotechnology Program at Rutgers University and the University of Medicine and Dentistry, New Jersey. Worked on heterologous expression of the beta-amyloid precursor protein.

Student and Trainee Supervision and Advising

Dissertation/Thesis Committee Chair or Co-Chair

University of Mississippi, Department of BioMolecular Sciences

- Niloofar Abolhasani Khaje (2016 – present)
- Hao Liu (2016 – present)
- Mohammad Riaz (2016 – 2019)
- Zhi Selina Cheng (2018 – present)

University of Georgia, Department of Chemistry

- Qi Gao (Ph.D. conferred 2017)
- Boer Xie (Ph.D. conferred 2016)
- Zixuan Li (Ph.D. conferred 2016)
- Yulun Chiu (Ph.D. conferred 2015, Institute of Bioinformatics, University of Georgia)

- Rongrong Huang (Ph.D. conferred 2014)
- Caroline Watson (Ph.D. conferred 2012)
- Jessica Saladino (M.S. conferred, 2011)
- ViLinh Tran (M.S. conferred, 2010)
- David Fischler (2012 – 2015; transferred)
- Tong Zhang (2014 – 2015; transferred)

Dissertation Committee Member

University of Mississippi

- Taisen Hao, BioMolecular Sciences (Ph.D. conferred 2017)
- Disha Prabhu, BioMolecular Sciences (2017 – present)
- Hanan Albataineh, BioMolecular Sciences (2018 – present)
- Zhiqiang Gao, Chemistry (2019 – present)
- Maali Alshammari, BioMolecular Sciences (2019 – present)
- William Vignovich, BioMolecular Sciences (M.S. conferred, 2020)
- Alysia Gonzales, BioMolecular Sciences (2020 – present)

University of Georgia

- Amika Sood, Institute of Bioinformatics (Ph.D. conferred 2016)
- Josette Wilkes, Department of Chemistry (Ph.D. conferred 2016)
- Chengli Zong, Department of Chemistry (Ph.D. conferred 2016)
- Majors Badgett, Department of Chemistry (Ph.D. conferred 2017)
- Emily Betchy, Department of Chemistry (Ph.D. conferred 2017)
- Joshua Driver, Department of Chemistry (Ph.D. conferred 2017)
- Isaac Agyekum, Department of Chemistry (Ph.D. conferred 2017)
- Morgan Stickney, Department of Chemistry (Ph.D. conferred 2020)
- Yuejie Zhao, Department of Chemistry (Ph.D. conferred 2017)
- David Fischler, Department of Chemistry (Ph.D. conferred 2019)
- Jiana Duan, Department of Chemistry (Ph.D. conferred 2018)

Other Post-Baccalaureate Mentorship

- Emily Hart (visiting graduate student, Department of Pharmaceutical Sciences, University of Maryland at Baltimore) 2018
- Christoph Schröder (visiting graduate student, Institute of Pharmacy, Martin Luther University, Halle-Wittenberg, Germany) 2015
- Dandan Zhou (visiting postdoctoral scholar) 2013
- Chelsea Pratt and Brad Vanderwielen (visiting application scientists from Bio-Rad for training on SEC-MALS) 2019

Postdoctoral Research Associates and Staff

- Anter Shami, B.S. (2019 – present)
- Sandeep Misra, Ph.D. (2015 – present)
- Charles Mobley, Ph.D. (2015 – present)
- Quntao Liang, Ph.D. (2016 – 2018)

- Surendar Tadi, Ph.D. (2017 – present)
- Omnia Ismaiel, Ph.D. (2015)
- Xiaoyan Li, Ph.D. (2013 – 2015)

Undergraduate Research Assistants

University of Mississippi

- Ariel Wilson (2016)
- Tam Dinh (2016)
- Chelsea Suppinger (2015 – 2017)
- Sydney Watson (2016 – 2017)
- Joseph Mason (2016 – 2019)
- Lindsey Miller (2016 – 2018); Taylor Medal recipient
- Jontae Warren (2017 – 2018)
- Olivia Buquoi (2017 – 2019)
- Addison Roush (2017 – present); Goldwater Scholarship recipient
- Martin Biggs (2018 – present)
- Helen Claire McNulty (2020 – present)
- Elaine Morrow (2020 – present)

University of Georgia

- Aaron Purser (2013 – 2014)
- David Reehl (2014 – 2015)

Honors and Awards

The Journal of Biomolecular Techniques Outstanding Manuscript Award, 2019

University of Mississippi nominee, 2019 Blavatnik National Award for Young Scientists, Life Sciences division

New Investigator Research Award, University of Mississippi School of Pharmacy, 2018

Rho Chi Society, 2018

Intramural Research Training Award Recipient for the National Institute of Environmental Health Sciences, National Institutes of Health.

Delegate for Oak Ridge National Laboratory to the 53rd Annual Meeting of Nobel Laureates in Lindau, Germany.

Service to Scientific Community

2019: Member, MBIE College of Assessors for the 2019 Endeavour Fund, New Zealand Ministry of Business, Innovation & Employment

2019: Roundtable Facilitator for “Basics of Biophysical Tools in the Assessment of Protein HOS”, CASSS Higher Order Structure 2019, April 8 – 10, San Mateo, CA

2019: Breakout Discussion Moderator for “Repeatability and Reproducibility in Higher Order Structure Analysis”, 10th Annual Biotherapeutics Analytical Summit, March 4 – 8, Alexandria, VA

2018-2019: Member, American Society for Mass Spectrometry 2019 Research Awards Committee

2018: *Ad hoc* Reviewer for National Institutes of Health, Biomedical Technology Research Resources

2018: Scientific Reviewer, SLAC National Accelerator Laboratory

2018: Member, NSF Division of Chemistry Review Panel

2017-2018: Member, American Society for Mass Spectrometry 2018 Research Awards Committee

2017: Session Chair for “Biomolecular Dynamics: From Solution to the Gas Phase,” 1st Advancing Mass Spectrometry for Biophysics and Structural Biology Meeting, July 28th – August 1, Ann Arbor, Michigan

2013 – 2017: Extramural Peer Reviewer, Institut National de la Santé et de la Recherche Médicale (National Institute of Health and Medical Research), France

2013 – 2016: Hydrogen-Deuterium Exchange and Covalent Labeling Interest Group Chair, American Society for Mass Spectrometry

2014: *Ad hoc* reviewer for National Institutes of Health, Biological Chemistry and Macromolecular Biophysics IRG

2014: *Ad hoc* Reviewer for National Science Foundation Chemistry Division

2014: Reviewer for the National Fellowships Committee of Sigma Delta Epsilon, Graduate Women in Science

2013: Session Chair for “Proteomics and Protein Measurements”, ISPPP 33rd Symposium on the Separation and Characterization of Biologically Important Molecules, July 17 – 19, Boston, Massachusetts.

2012: Session Chair for “Carbohydrate Analysis: New Developments”, 2012 ASMS Conference on Mass Spectrometry and Allied Topics, May 23rd, Vancouver, Canada.

2010 – 2012: FTMS Interest Group Chair, American Society for Mass Spectrometry

2011: Reviewer for the National Center for Research Resources, National Institutes of Health

2015 – present: Referee for Mississippi Region VII Science Fair: Lower Division

Invited journal referee

- Analyst
- Analytical and Bioanalytical Chemistry
- Analytical Chemistry
- Analytical Methods
- Angewandte Chemie
- Biochemistry
- Bioconjugate Chemistry
- Chemical Science
- Journal of the American Chemical Society
- Journal of the American Society for Mass Spectrometry
- Journal of Chromatography A
- Journal of Natural Products
- Journal of Physical Chemistry
- Journal of Proteome Research
- Journal of Visualized Experiments
- Methods
- Molecular and Cellular Proteomics
- Scientific Reports
- The FEBS Journal
- Toxicological Sciences

Service to University

University of Mississippi

Faculty Mentor for Prof. Sudeshna Roy, 2019 – present

Faculty Mentor for Prof. Vitor Pomin, 2019 – present

BioMolecular Sciences, Faculty Search Committee Member, Medicinal Chemistry/Computational Chemistry, 2019 – 2020

BioMolecular Sciences, Mentoring Task Force Head, 2019

Chancellor's Standing Committee Research Board: School of Pharmacy representative, 2019 – 2022

BioMolecular Sciences, Faculty Search Committee Member, Medicinal Chemistry/Computational Chemistry, 2017 – 2018

PI, University of Mississippi Phase I COBRE submission: "GlyCORE: Glycomics Center of Research Excellence", Jan 2018 submission date, Jan 2019 resubmission date

Member, Research and Graduate Affairs Committee, 2017 – present

Vice-Chair, Research and Graduate Affairs Committee, 2016 – 2017

BioMolecular Sciences, Department Chair Search Committee Member, 2016
BioMolecular Sciences, Faculty Search Committee Member, Pharmacognosy/NMR, 2016
BioMolecular Sciences, Faculty Search Committee Member, Pharmacology, 2015 – 2016
Member, Continuing Education, Lecture, and Alumni Activities Committee, 2015 – 2016
Pharmacy School Program Interviewer, 2016 – present
Early-Entry Program Interviewer, 2015 – present

University of Georgia

Elected delegate for the University of Georgia University Council representing Non-Academic Ranked Faculty within the Office of the Vice-President for Research, 2009 – 2012

Grants

Ongoing:

NIH P20GM130460-01A1 (Sharp, Ross) 05/15/20 – 03/31/25 5.4 calendar
Role: PI NIH/NIGMS \$7.5 million total (direct)

GlyCORE: Glycoscience Center of Research Excellence

The major goal of this project is the establishment of a new Phase I COBRE center focused on glycoscience as related to human health. GlyCORE will support investigators in glycoscience through direct funding of selected research projects, establish mentors for early career investigators, support the recruitment of new faculty in glycoscience, and develop local and regional meetings for investigators to discuss their work. GlyCORE will also support the establishment of three central research cores to support these investigators with cutting-edge biomedical research tools.

University of Mississippi Disaster Resilience Constellation Seed Grant: COVID-19 Track (Sharp) 05/12/20 – 06/26/20 0 calendar

Role: PI Univ. of Miss. \$2,500 total

Safety of New COVID-19 Inhibitors for Nasal Prophylaxis

The major goal of this seed grant proposal is to test the toxicity of four heparin derivatives in a mouse model via intranasal administration. Compounds are tested for nasal irritation, bleeding, discharge, weight loss, anoxia, and serum anti-coagulation.

R01 GM127267 (Sharp) 06/01/18 – 05/31/22 2 calendar
Role: PI NIH/NIGMS \$1.8 million total (direct)

Molecular Structure Determination by Mass Spectrometry and Computational Modeling

The major goals of this project are to develop and test the capabilities of multi-point high resolution hydroxyl radical protein footprinting coupled with computational modeling to accurately determine the structure of proteins with no homologs of known structure, as well as to develop HR-HRPF technology for use in integral membrane proteins.

R15 AI137996-01A1 (Stevens) 9/1/2019 – 8/31/2022 0.48 calendar

Role: Co-I NIH/NIAID \$88,537 (direct total year 1)
Myxobacterial Predatory Antimicrobial Production in Response to Quorum Sensing Signal Interception

The major goals of this project are to probe the production of new secondary metabolite chemical entities by myxobacterial cultivars in response to the induction of myxobacterial predation by exposure to prey quorum sensing molecules.

NIH 2 R01 DK042667 (Dahms) 12/01/2019 – 11/30/2024 1 calendar
Role: Co-I NIH/NIDDK \$256,060 (Sharp direct total)
Structural Analysis of the Mannose 6-Phosphate Receptors

The major goals of this project are to characterize the structure of the cation-independent mannose 6-phosphate receptor extracellular region, both alone and complexed with various biologically-important ligands. We will also probe the pH-dependent conformational changes that drive the biological activity of the receptor in the lysosome.

NIH R03NS110996 (Pomin) 04/1/2019 – 03/31/2021 0 calendar
Role: Co-I NIH/NINDS \$50,000 (direct total year 1)
Disruption of CS/KSPG-Mediated Neuronal Outgrowth Inhibition

The major goals of this project are to test the ability of various sulfated polysaccharides to reverse glycosaminoglycan-mediated inhibition of neuronal outgrowth that can occur at the glial scar, and to develop new technologies for sequencing sulfation patterns of keratan sulfate

Pending:

NIH R01 GRANT13161831 (Tandon) 08/03/20 – 08/02/25 0.6 calendar
Role: Co-I NIH/NIGMS \$3.3 million total (direct)
Targeting Heparan Sulfate in SARS-CoV-2 Infection

The major goals of this project are to understand the role of heparan sulfate as an attachment co-receptor for SARS-CoV-2, and to test the pharmacological properties of heparin and other sulfated polysaccharides to inhibit SARS-CoV-2 infection via intranasal prophylaxis using both *in vitro* and animal models.

NIH T32 GM141876-01 (PD/PI Majumdar, S) 06/01/21 – 05/31/26 0 calendar
Role: Mentor NIH/NIGMS \$2,149,560 total (direct)
G-RISE at The University of Mississippi

The goal of the ITPD3 Program is to increase diversity in the biomedical research workforce and to prepare strong Ph.D. graduates who are well-prepared to enter a career in the drug and device development fields.

Completed:

P41 GM103390 (Moremen) 02/01/2015 – 01/31/2020 2.0 calendar
NIH/NIGMS \$128,900/year (direct, Sharp only)
Research Resource for Integrated Glycotechnology

The major goals of this research resource are to develop and disseminate new technology for studying glycosaminoglycans and the structure and function of glycosaminoglycan-protein complexes.

Role: Co-Investigator, Projects 1 and 2 (subaward)

1608685 (Sharp) 09/01/16 – 08/31/20 0.72 calendar
NSF/CHE \$339,000 (total)

Measuring Protein Topology in Conformationally Heterogeneous Mixtures by Top-Down Hydroxyl Radical Protein Footprinting

The major goal of this project is the development and evaluation of high resolution hydroxyl radical protein footprinting using electron transfer dissociation of intact proteins to allow for the structural characterization of multiple conformations of a single protein sequence co-existing in solution.

Role: Principal Investigator

R43GM126617-01 (Weinberger) 01/01/18 – 12/31/18 Contractual
NIH/NIGMS \$223,704 (total)

Foxware™, an Advanced Data Analysis Package for Hydroxyl Radical Footprinting Higher Order Structural Analysis

The major goal of this SBIR project are to develop a alpha-version of a user-friendly software for analyzing covalent labeling data, annotating LC-MS peaks, and disseminating results into reports on structural changes

Role: Other Key Personnel (Analytical Support, CTO)

R43GM128486-01 (Persoff) 04/01/18 – 03/31/19 Contractual
NIH/NIGMS \$150,200 (direct)

Metal-oxide Photo-Oxidation of Proteins (MoPOP) for Biopharmaceutical Higher Order Structure Analysis

The major goals of this project are to create a new and preferred means of performing flash photo-oxidation of proteins without the use of hydrogen peroxide to enable hydroxyl radical protein foot-printing as used for biopharmaceutical higher order structural analysis.

Role: Other Key Personnel (Analytical Support, CTO)

R01 GM096049A (Sharp) 07/01/2012 – 06/30/2018 1 calendar
NIH/NIGMS \$190,000/year (direct)

Improved Hydroxyl Radical Footprinting for Modeling Protein Structure

The major goals of this project are to develop methods for generating amino acid solvent accessible surface area values from hydroxyl radical protein footprinting, and to use these technologies to develop models of the interaction between gp120 of HIV and a set of broadly neutralizing antibodies

Role: Principal Investigator

R43GM125420-01 (Weinberger) 09/01/17 – 08/31/18 Contractual
NIH/NIGMS \$224,995 (total)

Tailoring the Hydroxyl Radical Footprinting Approach to Provide a Solution for the Higher Order Structural Analytical Needs of the Biopharmaceutical Industry

The major goals of this SBIR project are to develop a stand-alone prototype instrument to perform Fast Photooxidation of Proteins chemistry, creating a single vendor solution for covalent labeling photochemistry to support the biopharmaceutical industry

Role: Other Key Personnel (Analytical Support, CTO)

9P20GM104932 (McCurdy) 09/01/2015 – 08/31/2017 0 calendar
NIH/NIGMS \$25,000/year (direct, Sharp only)

Center for Research Excellence in Natural Products Neuroscience (CORE-NPN)

The major goal of this pilot project under the CORE-NPN COBRE center is to investigate the potential of hydroxyl radical small molecule footprinting as a rapid *in vitro* screening tool for identifying ligands from a pool of natural products.

Role: Pilot Project Principal Investigator

1 R43 GM109602-01 (Leach) 04/01/2014 – 03/31/2017 0 calendar
NIH/NIGMS

Automated Conformational Analysis of Pharmaceutical Proteins

The major goals of this project are to develop and commercialize an automated platform for performing high-throughput hydroxyl radical protein footprinting analyses of protein pharmaceuticals for rapid conformational equivalency testing.

Role: Co-Investigator

5 R01 AI 077569-03 (Maier) 12/01/2008 – 11/31/2013
2.0 calendar
NIH/NAIAD \$20,000/year (direct, Sharp only)

Amino Acid Repair in *Helicobacter pylori*

The major goals of this project are to determine the amino acids recognized and repaired by the methionine sulfoxide reductase protein in *H. pylori* for various proteins in the oxidative stress response pathway.

Role: Subcontractor

R01GM061268 (Prestegard) 01/01/11 – 12/31/14
0 calendar (to be funded up to 1 calendar as project demands)
NIH/NIGMS \$8,151/year (direct, Sharp only)

NMR Approaches to Membrane Associated ARF Structures

The major goals of this project are to determine the structure of ARF associated with cell membranes, using primarily state-of-the-art NMR techniques.

Role: MS support

1R43 GM100634-01A1 (Becker) 09/11/2012-04/10/2014
0.24 calendar
NIH/NIGMS \$40,000/year (direct, Sharp only)

Byologic: Software for Mass Spectrometric Protein Drug Assays

The major goals of this project are to develop commercial software that will improve our ability to characterize the detailed composition of therapeutic proteins.

Role: Co-Investigator

R01GM033225 (Prestegard)

04/01/09 – 03/31/13

0 calendar (to be funded up to 2 calendar as project demands)

NIH/NIGMS

\$16,200/year (direct, Sharp only)

NMR of Cell Surface Oligosaccharides

The major goals of this project are the characterization of oligosaccharide conformation in solution, bound to protein and bound to membrane surfaces using newly developed NMR methods. Target systems include glycans on glycol-proteins that mediate protein-protein interactions.

Role: MS Support

Office of the Vice President of Research, University of Georgia Faculty Research Grant in the amount of \$12,105 awarded for January 2009-January 2011. Supports preliminary research into oxidation-induced conformational changes in Spo0F and improved tandem mass spectrometry for determining sites of oxidation.

Professional Societies

Member, American Society for Mass Spectrometry

Member, American Chemical Society

Member, Society for Glycobiology

Patents and Patent Applications

1. US 62511571; PCT US 18/34682: Flash Photo-Oxidation Device and Higher Order Structural Analysis
2. US 62747247: Intrinsic Radical Dosimetry System and Methods for Improved Hydroxyl Radical Protein Foot-Printing Analysis of Biopharmaceuticals and Biological Molecules
3. US 62788219: In-Cell Radical Dosimetry System and Methods for Improved Hydroxyl Radical Foot-Printing In Vivo Analysis

Publications

Huang H., Zheng L., Mao J., Liang Q., Lin J., Jiang L., Liu S., **Sharp, J.S.**, and Wei Z. (2020) Structural analysis of glycosaminoglycans from *Oviductus ranae*. *Food Chem* (**in review**)

Misra S.K. and **Sharp J.S.** (2020) Hydroxyl Radical Protein Footprinting via Fast Photochemical Oxidation of Proteins for the Determination of Protein Topography Changes. *J Vis Exp* (**in review**)

Tandon R., **Sharp J.S.**, Zhang F., Pomin V.H., Ashpole N.M., Mitra D., Jin W., Liu H., Sharma P. and Linhardt R.J. (2020) Effective Inhibition of SARS-CoV-2 Entry by Heparin and Enoxaparin Derivatives. *Commun Biol.* (in review) *bioRxiv* preprint: <https://www.biorxiv.org/content/10.1101/2020.06.08.140236v1>

Liu H., Liang Q. and **Sharp J.S.** (2020) Peracylation coupled with tandem mass spectrometry for structural sequencing of sulfated glycosaminoglycans without depolymerization. *J Am Soc Mass Spectrom* (in review)

Liang Q. and **Sharp J.S.** “De novo Sequencing of Heparin/Heparan Sulfate Oligosaccharides by Chemical Derivatization and LC-MS/MS.” In *Glycosaminoglycans – Chemistry & Biology*, part of the *Methods in Molecular Biology* series (in review)

Abolhasani Khaje N. and **Sharp J.S.** (2020) Rapid Quantification of Peptide Oxidation Isomers from Complex Mixtures. *Anal Chem* **92**, 3834-3843
<https://pubs.acs.org/doi/abs/10.1021/acs.analchem.9b05268>

Adaikpoh B.I., Akbar S., Albatineh H., Misra S.K., **Sharp J.S.** and Stevens D.C. (2020) Myxobacterial Response to Methyljasmonate Exposure Indicates Contribution to Plant Recruitment of Micropredators. *Front Microbiol*
<https://doi.org/10.3389/fmicb.2020.00034>

Bezerra F.F., Vignovich W.P., Aderibigbe A.O., Liu H., **Sharp J.S.**, Doerksen R.J. and Pomin, V.H. (2020) Conformational properties of L-fucose and the tetrasaccharide building block of the sulfated L-fucan from *Lytechinus variegatus*. *J Struct Biol* **209**, 107407 <https://doi.org/10.1016/j.jsb.2019.107407>

Olson L.J., Misra S., Ishihara M., Battaile K., Grant O., Sood A., Woods R.J., Kim J.P., Tiemeyer M., Ren G., **Sharp J.S.** and Dahms N.M. (2020) Allosteric regulation of lysosomal enzyme recognition by the cation-independent mannose-6-phosphate receptor. *Commun Biol* (in review) *bioRxiv* preprint: <https://www.biorxiv.org/content/10.1101/2020.02.21.959957v1>

Roush A.E., Riaz M., Misra S.K., Weinberger S.R. and **Sharp J.S.** (2020) Intrinsic Buffer Hydroxyl Radical Dosimetry Using Tris(Hydroxymethyl)Aminomethane. *J Am Soc Mass Spectrom* **31**, 169-172 <https://pubs.acs.org/doi/abs/10.1021/jasms.9b00088>

Tadi S. and **Sharp J.S.** (2019) Top-Down ETD-MS Provides Unreliable Quantitation of Methionine Oxidation. *J Biomol Tech* **30**, 50-57
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6808186/>

***Received the Journal of Biomolecular Techniques Outstanding Manuscript Award for 2019**

Albatineh H., Duke M., Misra S.K., **Sharp J.S.** and Stevens D.C. (2019) Cryptic, Solo Acylhomoserine Lactone Synthase from Predatory Myxobacterium Suggests Beneficial

Contribution to Prey Quorum Sensing. *Appl Environ Microbiol* (in review) *bioRxiv* preprint: <https://www.biorxiv.org/content/10.1101/849075v1>

Tadi S. and **Sharp J.S.** (2019) Online Size Exclusion Chromatography-Fast Photochemical Oxidation of Proteins Allows for Targeted Structural Analysis of Conformationally Heterogeneous Mixtures. *bioRxiv* preprint: <https://doi.org/10.1101/825521>

Liu H., Joshi A., Chopra P., Boons, G-J., and **Sharp, J.S.** (2019) Salt-free fractionation of complex isomeric mixtures of glycosaminoglycan oligosaccharides compatible with ESI-MS and microarray analysis. *Sci Rep* **9**, 16566 <https://www.nature.com/articles/s41598-019-53070-z>

Misra S.K., Orlando R., Weinberger S.R. and **Sharp J.S.** (2019) Compensated Hydroxyl Radical Protein Footprinting Measures Buffer and Excipient Effects on Conformation and Aggregation in an Adalimumab Biosimilar. *AAPS J* **21**, 87 <https://link.springer.com/article/10.1208%2Fs12248-019-0358-2>

Hasan M.H., Parmar R.C., Liang Q., Qiu H., Tiwari V., **Sharp J.**, Wang L. and Tandon R. (2019) The Degree of Polymerization and Sulfation Patterns in Heparan Sulfate are Critical Determinants of Cytomegalovirus Infectivity. *bioRxiv* preprint: <https://doi.org/10.1101/590463>

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Li X., Grant O.C., Ito K., Wallace A., Wang S., Lu S., Woods R.J. and **Sharp J.S.** (2017) Structural Analysis of Glycosylated Native HIV-1 gp120-b12 Antibody Complex using Hydroxyl Radical Protein Footprinting. *Biochemistry* **56**, 957-970

Chiu Y., Schliekelman P., Orlando R. and **Sharp, J.S.** (2016) A Multivariate Mixture Model to Estimate the Accuracy of Glycosaminoglycan Identifications Made by MS/MS and Database Search. *Mol Cell Proteom* **16**, 255-264

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Xie B. and **Sharp J.S.** (2016) Relative Quantification of Sites of Peptide and Protein Modification Using Size Exclusion Chromatography Coupled with Electron Transfer Dissociation. *J Am Soc Mass Spectrom* **27**, 1322-1327

Huang R., Zong C., Venot A., Chiu Y., Zhou D., Boons G.J. and **Sharp J.S.** (2016) *De Novo* Sequencing of Complex Mixtures of Heparan Sulfate Oligosaccharides. *Anal Chem* **88**, 5299-5307

Xie B. and **Sharp J.S.** (2015) Hydroxyl Radical Dosimetry for High Flux Hydroxyl Radical Protein Footprinting Applications Using a Simple Optical Detection Method. *Anal Chem* **87**, 10719-10723

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Watson C. and **Sharp J.S.** (2012) Conformational analysis of therapeutic proteins by hydroxyl radical protein footprinting. *AAPS J* **14**, 206-217

Wang X., Watson C., **Sharp J.S.**, Handel T.M. and Prestegard J.H. (2011) Oligomeric Structure of the Chemokine CCL5/RANTES from NMR, MS, and SAXS Data. *Structure* **19**, 1138-1148

Sharp J.S. (2011) Quantitative and qualitative analysis of post-translationally modified proteins. In R.A. Meyers (Ed) *Encyclopedia of Analytical Chemistry*. John Wiley & Sons, Inc.

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- Gau B.C., **Sharp, J.S.**, Rempel D.L., and Gross M.L. (2009) Fast photochemical oxidation of proteins footprints faster than protein unfolding. *Anal Chem* **81**, 6563-6571
- Saladino J., Liu M., Live D., and **Sharp, J.S.** (2009) Aliphatic peptidyl hydroperoxides as a source of secondary oxidation in hydroxyl radical protein footprinting. *J Am Soc Mass Spectrom* **20**, 1123-1126
- Watson C., Janik I., Zhuang T., Charvátová O., Woods R.J. and **Sharp J.S.** (2009) Pulsed electron beam water radiolysis for sub-microsecond hydroxyl radical protein footprinting. *Anal Chem* **81**, 2496-2505
- Charvátová O., Foley B.L., Bern M.W., **Sharp J.S.**, Orlando R., Woods R.J. (2008) Quantifying protein interface footprinting by hydroxyl radical oxidation and Molecular Dynamics simulation: Application to galectin-1. *J. Am. Soc. Mass Spectrom.* **19**, 1692-1705
- Smedley J.G., **Sharp J.S.**, Kuhn J.F., Tomer K.B. (2008) Probing the pH-dependent prepore to pore transition of *Bacillus anthracis* protective antigen with differential oxidative protein footprinting. *Biochemistry.* **47**, 10694-10704
- Venkatesh, S., Tomer, K.B., **Sharp, J.S.** (2007) Rapid identification of oxidation-induced conformational changes by kinetic analysis. *Rapid Commun Mass Spectrom* **21**, 3927-3936
- Sharp, J.S.** and Tomer, K.B. (2007) Analysis of the oxidative damage-induced conformational changes of apo- and holo-calmodulin by dose dependant protein oxidative surface mapping. *Biophys J* **92**, 1682-1692.
- Sharp, J.S.** and Tomer, K.B. (2006) Effects of Anion Proximity in Peptide Primary Sequence on the Rate and Mechanism of Leucine Oxidation. *Analytical Chemistry* **78**, 4885-4893.

Sharp, J.S., Sullivan, D.M., Cavanagh, J., and Tomer, K.B. (2006) Measurement of multi-site oxidation kinetics reveals an active site conformational change in Spo0F as a result of protein oxidation. *Biochemistry* **45**, 6260-6266.

Sharp, J.S., Nelson, S., Brown, D.T., and Tomer, K.B. (2006) Structural characterization of E2 glycoprotein of Sindbis by lysine biotinylation and LC-MS/MS. *Virology* **348**, 216-223.

Sharp, J.S. and Tomer, K.B. (2005) Formation of $[b_{(n-1)} + OH + H]^+$ ions by solution-phase chemistry. *Journal of the American Society for Mass Spectrometry* **16**, 607-621.

Sharp, J.S., Guo, J., Uchiki, T., Xu, Y., Dealwis, C., and Hettich, R.L. (2005). Photochemical surface mapping of C14S-Sml1p for constrained computational modeling of protein structure. *Analytical Biochemistry* **340**, 201-212.

Sharp, J.S., Becker, J.M., and Hettich, R.L. (2004) Analysis of protein solvent accessible surfaces by photochemical oxidation and mass spectrometry. *Analytical Chemistry* **76**, 672-683.

VerBerkmoes, N., **Sharp, J.S.**, and Hettich, R.L. (2004) Mass Spectrometry. In *Microbial Functional Genomics* (eds. J. Zhou, D.K. Thompson, Y. Xu, and J.M. Tiedje), Ch. 9, pg 241-283. John Wiley & Sons, Hoboken, NJ.

Sharp, J.S., Becker, J.M., and Hettich, R.L. (2002) Protein surface mapping by chemical oxidation: structural analysis by mass spectrometry. *Analytical Biochemistry* **313**, 216-225.

Koh, S., Wiles, A.M., **Sharp, J.S.**, Naider, F.R., Becker, J.M., Stacey, G. (2002) An oligopeptide transporter gene family in Arabidopsis. *Plant Physiology* **128**, 21-29.

Invited Lectures

2020 SciX 2020, Photons in Mass Spectrometry, October 11th – 16th, Reno, Nevada (invitation accepted)

“New Tools for Probing Protein-Glycosaminoglycan Interactions.” **2020** University of Mississippi Medical Center, Neurobiology Seminar Series, April 14th, Jackson, Mississippi (invitation accepted)

“Clarity from Complexity: Probing Protein-Glycosaminoglycan Interactions Using Mass Spectrometry.” **2019** University of Massachusetts Department of Chemistry, October 17th, Amherst, Massachusetts

“FOX: Laser-Free Sub-Millisecond Broadband Flash Oxidation for HRPFF.” **2019** Advancing Mass Spectrometry Meeting, July 21-25, Amherst, Massachusetts

“Compensated Hydroxyl Radical Protein Footprinting: A Flexible, Quantitative Probe of Protein Topography.” **2019** 8th International Symposium on Higher Order Structure of Protein Therapeutics (HOS 2019), April 8-10, San Mateo, California

“Qualitative and Quantitative Measurements of Protein Topography by Hydroxyl Radical Protein Footprinting.” **2019** 10th Annual Biotherapeutics Analytical Summit, March 4-8, Alexandria, Virginia

“Reproducibility and Robustness in FPOP: the Need for Community Standards for Radical Dosimetry.” **2019** ASMS Sanibel Meeting on Chemical Cross-Linking and Covalent Labeling: From Proteins to Cellular Networks, January 24-27, St. Petersburg, Florida

“Probing Protein-Glycosaminoglycan Interactions Using Mass Spectrometry: Extracting Clarity from Complexity.” **2018** Virginia Commonwealth University Institute for Structural Biology, Drug Discovery and Development, May 2nd, Richmond, Virginia

“High Resolution Hydroxyl Radical Protein Footprinting: Moving Towards Structural Determination.” **2018** University of Kansas Department of Chemistry, March 16, Lawrence, Kansas

“Quantitative Protein Topography Measurements by High Resolution Hydroxyl Radical Protein Footprinting.” **2017** Genentech, Inc. December 14th, San Francisco, California

“High Resolution Hydroxyl Radical Footprinting: Integrating Molecular Modeling with Covalent Labeling LC-MS.” **2017** 37th International Symposium and Exhibit on the Separation of Proteins, Peptides and Polynucleotides, July 19-21, Philadelphia, Pennsylvania

“Hydroxyl Radicals as Quantitative Probes for Protein Topography.” **2017** North Carolina State University Department of Chemistry, January 13, Raleigh, North Carolina

“Hydroxyl Radical Protein Footprinting: Structural Biology by the Masses.” **2015** University of Mississippi Department of Chemistry, October 8, Oxford, Mississippi

“Progress Towards Automated Sequencing of Heparin/Heparan Sulfate.” **2013** 33rd Symposium on the Separation and Characterization of Biologically Important Molecules, July 17-July 19, Boston, Massachusetts

“Hydroxyl Radical Protein Footprinting: A Mass Spectrometry-Based Measurement of Protein Conformation and Ligand Binding.” **2010** The University of Georgia College of Pharmacy, September 30, Athens, Georgia

“Structural Analysis of Mixtures of Chondroitin Sulfate.” **2009** Waters Corporation, November 3 and November 5, Beverly, Massachusetts

“Hydroxyl Radical Footprinting: A Versatile Probe of Protein Structure” **2008** University of Notre Dame Radiation Laboratory, June 23, South Bend, Indiana

“Hydroxyl Radical Footprinting: A Versatile Probe of Protein Structure and Folding.” **2007** Atlanta Area Mass Spectrometry Discussion Group, October 22, Athens, Georgia.

“Hydroxyl Radical Footprinting and Oxidation-Induced Conformational Change: Cautionary Tales for Covalent Labelers.” **2007** Hydrogen Exchange and Covalent Labeling Interest Group, 55th Annual ASMS Conference on Mass Spectrometry, June 3 - June 7, Indianapolis, Indiana

“New methods for characterizing the structural consequences of radical-mediated protein oxidation.” **2007** University of North Carolina Department of Biochemistry and Biophysics, January 16, Chapel Hill, North Carolina.

“Probing structural changes due to oxidative damage in proteins.” **2006** Vanderbilt Institute of Chemical Biology, December 20, Nashville, Tennessee

Accepted Oral Presentations at Regional, National, and International Meetings

Misra S.K., Sood A., Soares P.A., Pomin V.H., Woods R.J. and **Sharp J.S. 2018** Identification of the Fondaparinux Binding Site of JR-FL gp120 by High Resolution Hydroxyl Radical Protein Footprinting and Blind Computational Docking. 66th Annual ASMS Conference on Mass Spectrometry and Allied Topics, June 3-June 7, San Diego, California

Li Z., Moniz H., Wang S., Ramiah A., Zhang F., Moremen, K.W., Linhardt R.J. and **Sharp J.S. 2015** ETD-Based High Spatial Resolution Hydroxyl Radical Protein Footprinting Reveals an Extended Robo1-Heparin Binding Interface. 63rd Annual ASMS Conference on Mass Spectrometry, May 31-June 4, St. Louis, Missouri

Huang R., Condac E., Chiu Y., Heiss C., Ishihara, M. Kailemia M.J., Amster J., Azadi P., Wang L. and **Sharp J.S. 2013** Semi-automated sequencing of affinity-purified heparan sulfate oligosaccharides. 2013 61st Annual ASMS Conference on Mass Spectrometry, June 9-June 13, Minneapolis, Minnesota

Huang R. and **Sharp J.S. 2012** Sequencing of Mixtures of Heparin/Heparan Sulfate Oligomers by Chemical Derivatization and LC-MS/MS. 4th Charles Warren Workshop, August 8-11, Athens, Georgia

Sharp J.S. 2012 Towards Quantitative Interpretations of Hydroxyl Radical Footprinting Data. Hydrogen Exchange and Covalent Labeling Interest Group, 60th ASMS Conference on Mass Spectrometry and Allied Topics, May 20-24, Vancouver, British Columbia, Canada

Watson C. and **Sharp J.S.** **2012** Rapid Conformational Analysis of Protein Pharmaceuticals by an Abbreviated Hydroxyl Radical Footprinting Method. 60th ASMS Conference on Mass Spectrometry and Allied Topics, May 20-24, Vancouver, British Columbia, Canada

Huang R. and **Sharp J.S.** **2011** Separation and Structural Characterization of Glycosaminoglycan Oligomers by LC-MSⁿ Using a Chemical Derivatization Strategy. 2011 International Symposium on the Separation of Proteins, Peptides & Polynucleotides, October 26, Alexandria, Virginia.

Huang R., Pomin V.H. and **Sharp J.S.** **2011** A Chemical Derivatization Strategy for Structural Analysis of Isomeric Glycosaminoglycan Oligosaccharides Using Reverse Phase LC-MSⁿ. 59th ASMS Conference on Mass Spectrometry and Allied Topics, June 5-9, Denver, Colorado

Watson C., Wang X., **Sharp J.S.** and Prestegard J.H. **2011** Novel structural model for CCL5 (RANTES) oligomerization using hydroxyl radical footprinting. 59th ASMS Conference on Mass Spectrometry and Allied Topics, June 5-9, Denver, Colorado

Watson C., Wang X., Pomin V.H., Prestegard J.H. and **Sharp J.S.** **2011** Structural Investigation of CCL5 Protein and CCL5-Glycosaminoglycan Complex Using Mass Spectrometry. 61st Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, March 13-18, Atlanta, Georgia

Saladino J. and **Sharp J.S.** **2011** Identifying and Quantifying Hydroxyl Radical Oxidation Products in Peptides and Proteins Using Improved Mass Spectrometric Techniques. 61st Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, March 13-18, Atlanta, Georgia

Huang R. and **Sharp J.S.** **2010** Structure Analysis of Derivatized Chondroitin Sulfate Oligomers with CID MS/MS. Glycomics and Glycoproteins Interest Group, 58th Annual ASMS Conference on Mass Spectrometry, May 23-May 27, Salt Lake City, Utah (given by Ms. Rongrong Huang in my absence)

Watson C. and **Sharp J.S.** **2010** Application of Isotope Labeling Techniques in Protein Footprinting Studies. **2010** Hydrogen Exchange and Covalent Labeling Interest Group, 58th Annual ASMS Conference on Mass Spectrometry, May 23-May 27, Salt Lake City, Utah (given by Ms. Caroline Watson in my absence)

Saladino J. and **Sharp J.S.** **2009** Improving Techniques for the Detection and Quantification of Oxidized Amino Acids in Peptides and Proteins. 10th Athens-Atlanta Mass Spectrometry Discussion Group Summer Symposium, October 6-October 7, Atlanta, Georgia

C. Yu F., Prestegard J. and **Sharp J.S.** **2009** A Hydroxyl Radical Protein Footprinting Approach to the Structure of CCL5-Chondroitin Sulfate (CS) Complex. 10th Athens-

Atlanta Mass Spectrometry Discussion Group Summer Symposium, October 6-October 7, Atlanta, Georgia

Watson C., Yu F., Prestegard J. and **Sharp, J.S.** **2009** Hydroxyl Radical Footprinting of CCL5-Chondroitin Sulfate Complex Reveals both the Binding Interface and a Ligand-Induced Conformational Change. 57th ASMS Conference on Mass Spectrometry and Allied Topics, May 31-June 4, Philadelphia, Pennsylvania.

Watson C., O'Donnell D., Janik I., Orlando R. and **Sharp J.S.** **2008** Demonstration of a Novel Methodology for Sub-Microsecond Hydroxyl Radical Protein Footprinting by Electron Beam Pulse Water Radiolysis. 59th Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, March 1-7, New Orleans, Louisiana.

Sharp J.S. and Tomer K.B. **2004** Structural characterization of $[b_{(n-1)}+OH + H]^+$ ions by solution phase chemistry and mass spectrometry. 2004 Southeastern Regional Meeting of the American Chemical Society, November 10-13, Research Triangle Park, North Carolina.

Sharp J.S. and Tomer K.B. **2004** Solution-phase formation of $b_{(n-1)}+H_2O$ peptide ions for position-specific fragmentation at the C-terminus. 52nd Annual Conference on Mass Spectrometry and Allied Topics, May 23-27, Nashville, Tennessee.

Sharp J.S., Guo J., Gupta V., Uchiki T., Ellrott K., Becker J.M., Xu D., Xu Y., Dealwis C., and Hettich R.L. **2003** Photochemical protein surface mapping as an indicator of computational structure model accuracy. 51st Annual Conference on Mass Spectrometry and Allied Topics, June 8-12, Montreal, Canada.

Sharp J.S., Becker J.M., and Hettich R.L. **2002** Characterization of protein structure by chemical oxidation and mass spectrometry. Student Research Award Travel Grant presentation for the East Tennessee Mass Spectrometry Discussion Group, Knoxville, Tennessee

Sharp J.S., VerBerkmoes N., Asano K., Becker J., and Hettich R. **2002** Integrated Proteome Characterization: Beyond Protein Identification. Southeastern Regional Yeast Meeting, March 8-10, Gatlinburg, Tennessee

Poster Presentations at Regional, National, and International Meetings

Over 100 poster presentations as first author or senior author at various regional, national, and international meetings.