BIOGRAPHICAL SKETCH

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NAME: Glass, Karen C.

eRA COMMONS USER NAME (credential, e.g., agency login): kchampag

POSITION TITLE: Associate Professor, Pharmaceutical Sciences

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Massachusetts (UMass), Amherst	B.S.	05/99	Microbiology
University of Vermont (UVM)	Ph.D.	10/05	Microbiology & Molecular Genetics, Christopher S. Francklyn
Rapid Data Collection and Structure Solving at the NSLS: A Practical Course in Macromolecular X-Ray Diffraction Measurement, Brookhaven, NY	Training Course	April 6-11, 2003	X-Ray Crystallography
University of California, Santa Cruz	Postdoctoral	11/06	MCD Biology, Harry F. Noller
NMRFAM Protein Structure Determination Workshop, University of Wisconsin-Madison	Training Course	June 6-11, 2010	Nuclear Magnetic Resonance
University of Colorado Denver (UCD)	Postdoctoral	08/10	Pharmacology, Tatiana G. Kutateladze

A. Personal Statement

The focus of my laboratory is to understand how epigenetic signaling regulates gene expression and how alterations in these pathways are involved in disease development. In particular, we are investigating the molecular mechanisms driving how chromatin reader domains recognize post-translational modifications on histone proteins. I have a strong background in Biochemistry and Molecular Biology, with specific training in Enzymology (using spectrometric and isothermal titration calorimetry binding assays), X-ray Crystallography and Nuclear Magnetic Resonance (NMR) techniques. We routinely use these techniques to investigate the protein-ligand interactions of chromatin reader domains with specifically modified histone peptides. However, we want to investigate the interaction of chromatin reader domains with post-translational modifications in a more chromatin relevant context (i.e. bound to modified nucleosomes). To do this we plan to take advantage of the recent advances in Cryo-EM to solve the structures of chromatin reader proteins in complex with recombinant nucleosomes. We have three main research projects that would benefit from access to Cryo-EM technology. 1. The BRPF1 protein is a structural protein in the MOZ/MORF histone acetyltransferase complex that contains three reader domains including a bromodomain (acetyllysine recognition), a PZP domain (DNA and unmodified histone H3 recognition), and a PWWP domain (DNA and methylated histone H3 recognition). 2. The ATAD2/B proteins contain a C-terminal bromodomain and an AAA ATPase domain, which have both been shown to be important for targeting these proteins to chromatin, and 3. Two bromodomain proteins from *Plasmodium falciparum*, PfBDP1 and PfBDP2, that together form a 181 kDa complex that binds acetylated histones to regulate the expression of invasion related genes. Obtaining structural information on these proteins in complex with the nucleosome will provide new insights into the molecular mechanisms of histone recognition in a chromatin dependent context. Since these proteins are significant contributors to the development of acute

myeloid leukemia, several cancers, and malaria pathogenesis, these studies will be important to delineate epigenetic signaling pathways that can be altered to prevent cancer proliferation and disease progression. Ultimately, these studies will lead to the identification of new therapeutics, more specific treatment strategies, and better overall outcomes for patients.

1. Carlson S and **Glass KC.** (2014) The MOZ Histone Acetyltransferase in Epigenetic Signaling and Disease. ***J Cell Physiol***. Nov 229(11): 1571-4. PMCID: PMC4750494.
2. Lloyd JT, **Glass KC**. (2018) Biological function and histone recognition of family IV bromodomain-containing proteins. ***J Cell Physiol***. 2018 Mar;233(3):1877-1886. doi: 10.1002/jcp.26010. Epub 2017 Jun 13. Review. PMCID: PMC5683942.
3. Obi JO, Lubula MY, Cornilescu G, Henrickson A, McGuire K, Evans CM, Phillips M, Boyson SP, Demeler B, Markley JL, **Glass KC**. (2020) The BRPF1 bromodomain is a molecular reader of di-acetyllysine. ***Curr Res Struct Biol.*** 2020;2:104-115. doi: 10.1016/j.crstbi.2020.05.001. Epub 2020 May 12. PMCID: PMC7861561.
4. Lloyd JT, McLaughlin K, Lubula MY, Gay JC, Dest A, Gao C, Phillips M, Tonelli M, Cornilescu G, Marunde MR, Evans CM, Boyson SP, Carlson S, Keogh MC, Markley JL, Frietze S, and **Glass KC**. (2020) Structural insights into the recognition of mono- and di-acetylated histones by the ATAD2B bromodomain. ***J. Med Chem***. 2020 Nov 12;63(21):12799-12813. doi: 10.1021/acs.jmedchem.0c01178. Epub 2020 Oct 21. PMCID: PMC7884259.

B. Positions and Honors

Positions and Employment

8/99-11/05	Graduate Research Associate, Department of Microbiology & Molecular Genetics, UVM, Burlington, VT (Christopher S. Francklyn).
11/05-11/06	Postdoctoral Research Associate, Department of Molecular, Cellular and Developmental Biology, UCSC, Santa Cruz, CA (Harry F. Noller).
11/06-08/10	Postdoctoral Research Fellow, Department of Pharmacology, UCD, Aurora, CO (Tatiana G. Kutateladze).
08/09-12/09	Affiliate Professor, Department of Biology, Metropolitan State College, Denver, CO.
08/10-05/16	Assistant Professor, Department of Pharmaceutical Sciences, Albany College of Pharmacy and Health Sciences (ACPHS), Vermont Campus.
08/11-06/19	Adjunct Assistant Professor, Department of Biochemistry, Larner College of Medicine, UVM.
05/16-present	Associate Professor, Department of Pharmaceutical Sciences, Albany College of Pharmacy and Health Sciences (ACPHS), Vermont Campus.
07/19-present	Adjunct Associate Professor, Department of Biochemistry, Larner College of Medicine, UVM.

Other Experience and Professional Memberships

2010-Present	Member, American Crystallographic Association
2011-Present	Member, American Society for Biochemistry and Molecular Biology
2011-Present	Member, University of Vermont Cancer Center
2013-Present	Member, UVM Graduate Faculty
2014-Present	Member, UVM Cellular, Molecular and Biomedical Sciences (CMB) Program
2021-Present	Member, Biophysical Society
Feb 2016	Ad Hoc Reviewer, NIH Molecular Genetics A Study Section (MGA)
Sept 2019	Ad Hoc Reviewer, NIH Molecular Genetics A Study Section (MGA)
June 2020	Ad Hoc Reviewer, NIH Fellowship: Genes, Genomes, and Genetics Study Section
March 2021	Ad Hoc Reviewer, NIH Fellowship: Genes, Genomes, and Genetics Study Section

Honors

1996	Alpha Lambda Delta, a national academic honors society for freshmen in the top 10% of their class, member.
1997	Golden Key National Honors Society, member.
1998	Honors Research Grant for undergraduate thesis research.
1999	Howard Hughes grant for undergraduate research.
1999	Graduated with honors, *Magna Cum Laude.*
2001	American Crystallography Association student travel grant, ACA meeting, Los Angeles, CA.

2001-03 Vermont Department of Energy Experimental Program to Stimulate Competitive Research (DOE EPSCoR) graduate research fellowship.
2004 Travel award from the UVM graduate college for a tRNA Synthetase conference, Seoul, Korea.
2008 American Heart Association, postdoctoral fellowship (declined).
2008 Keystone Symposia Scholarship, 'Molecular Basis for Chromatin Modifications and Epigenetic Phenomena', Snowmass, CO.
2008 Post-Doctoral Award for Outstanding Achievement, Department of Pharmacology, UCD, SOM.
2010 Poster presentation award. University of Colorado Denver Postdoctoral Research Day.
2010 Poster presentation award winner in the Faculty/Staff category. Vermont Cancer Center's 2010 Clinical and Translational Research Symposium: Inflammation & Cancer.
2011 Poster presentation award winner in the Faculty/Staff category. Vermont Cancer Center's 2011 Clinical and Translational Research Symposium: DNA Repair & Cancer.
2012 ASBMB annual meeting thematic best poster in the Gene Regulation category
2014 ACPHS Researcher of the Year award

C. Contribution to Science (Please note name change in 2009 from Champagne KS to Glass KC)

1. **Allosteric regulation of histidine biosynthesis:** As a graduate student in the laboratory of Dr. Christopher S. Francklyn at UVM I characterized the structure and function of the N1-5'-phosphoribosyl ATP transferase (ATP-PRTase) in *Lactococcus Lactis*, which catalyzes the first step of histidine biosynthesis. The *L. lactis* ATP-PRTase ezyme is unique and contains two subunit types, one of which is a paralogous to histidyl-tRNA synethtase (HisRS). I established that the HisZG ATP-PRTase from *L. lactis* is a 250 kDa multimeric enzyme complex consisting of four HisG and four HisZ subunits using size exclusion chromatography, and quantitative protein sequencing. Under the guidance of Dr. Sylvie Doublié and Dr. Stephen J. Everse I solved the first structure of a PRPP-bound ATP-PRTase, and provided a structural model for its allosteric activation by comparing inhibited and activated versions of ATP-PRTs from both the hetero-octameric and hexameric families. Mutational analysis followed by kinetic binding assays identified the histidine binding sites in a region highly conserved between HisZ and the functional HisRS, confirming the role of HisZ as a regulatory subunit in the *L. lactis* ATP-PRTase. My research provided evidence on how a histidyl-tRNA synthetase-like domain evolved through evolution to function as a regulatory domain in amino acid biosynthesis.

    a. Bovee ML, **Champagne KS**, Demeler B, Francklyn CS. (2002) The Quaternary Structure of the HisZ-HisG N-1-(5'-Phosphoribosyl)-ATP Transferase from *Lactococcus lactis.* ***Biochemistry*****.** 41(39): 11838-11846. PMID: 12269828.

    b. **Champagne KS**, Sissler M, Larrabee Y, Doublié S, Francklyn CS. (2005) Activation of the hetero-octameric ATP phosphoribosyl transferase through subunit interface rearrangement by a tRNA synthetase paralog. ***J Biol Chem****.* 280(40): 34096-34104. PMID: 16051603.

    c. **Champagne KS**, Piscitelli E, Francklyn CS. (2006) Substrate recognition by the hetero-octameric ATP phosphoribosyltransferase from *L. lactis*. ***Biochemistry****.* 45(50): 14933-43. PMID: 17154531.

2. **Molecular mechanisms of histone recognition by the plant homeodomain (PHD):** I became interested in the field of Epigenetics and wanted to understand how the 'histone code' might extend and modify our genetic (DNA) information to regulate key cellular processes. Modifications on the histone tail have been shown to be important in altering chromatin structure, and they regulate gene expression by facilitating access of DNA-binding transcription factors. Modifications to the histone tail also act as markers, allowing non-histone proteins to interact with the chromatin. When I began my postdoctoral training with Tatiana G. Kutateladze the molecular basis of histone recognition by chromatin reader domains was poorly understood. I made several seminal discoveries during this period. Using tryptophan fluorescence I revealed that there is cross-talk between adjacent histone modifications on the histone H3 tail that regulate the functions of proteins interacting with these marks. We showed that di-methylation of arginine 2 on histone H3 (H3R2me2) modulates the interaction of the RAG2 PHD finger with tri-methylated lysine 4 (H3K4me3) on the histone tail, and is essential for V(D)J recombination. I also demonstrated the molecular mechanism of H3K4me3 recognition by the Inhibitor of Growth PHD fingers is conserved within this family, and that histone binding both recruits and activates ING4/5-associated histone acetyltransferase complexes on chromatin. My research also revealed that PHD fingers are divided into sub-families based on their selection of different ligands including unmodified histone H3, and acetylated or methylated lysine.

a. Matthews AG, Kuo AJ, Ramón-Maiques S, Han S, **Champagne KS**, Ivanov D, Gallardo M, Carney D, Cheung P, Ciccone DN, Walter KL, Utz PJ, Shi Y, Kutateladze TG, Yang W, Gozani O, Oettinger MA. (2007) RAG2 PHD finger couples histone H3 lysine 4 trimethylation with V(D)J recombination. ***Nature***. Dec 13; 450(7172): 1106-10. PMCID: PMC2988437.

b. **Champagne KS**, Saksouk N, Peña PV, Johnson K, Ullah M, Yang XJ, Côté J, Kutateladze TG. (2008) The crystal structure of the ING5 PHD finger in complex with an H3K4me3 histone peptide. ***Proteins***. 72(4): 1371-6. PMCID: PMC2756976.

c. Hung T*, Binda O*, **Champagne KS***, Kuo AJ, Johnson K, Chang HY, Simon MD, Kutateladze TG and Gozani O. (2009) ING4-mediated crosstalk between histone H3K4 trimethylation and H3 acetylation attenuates cellular transformation. ***Mol Cell.*** 33(2): 248-256 PMCID: PMC2650391.

d. Kim S, Natesan S, Cornilescu G, Carlson S, Tonelli M, McClurg UL, Binda O, Robson CN, Markley JL, Balaz S, **Glass KC**. (2016) Mechanism of Histone H3K4me3 Recognition by the Plant Homeodomain of Inhibitor of Growth 3. ***J Biol Chem***. Aug 26;291(35):18326-41. PMCID: PMC5000080.

3. **Molecular mechanisms of histone recognition by bromodomains:** In my independent research program I have continued studying the structure and function of chromatin reader domains, particularly bromodomains, which interact specifically with acetylated histones. The 61 human bromodomain-containing proteins have a wide variety of biological activities. However, while the structure of many of these bromodomain modules are solved, how these protein modules differentiate between multiple acetyllysine modifications to read the histone code is unknown. We recently established the molecular basis of histone acetyllysine recognition by the BRPF1 bromodomain and discovered that the BRPF1 bromodomain interacts with multiple acetylated histone peptides. We also solved the first bromodomain structure in complex with histone H2A acetylated at lysine 5 (H2AK5ac). These structural and mechanistic details of histone recognition by bromodomains is crucial for the development of new therapeutic interventions and molecular tools to study a variety of cancers, and has fundamentally advanced our understanding of how bromodomains recognize and select for acetyllysine marks.

   a. Poplawski A, Hu K, Lee W, Natesan S, Peng D, Carlson S, Shi X, Balaz S, Markley JL, **Glass KC**. (2014) Molecular Insights into the Recognition of N-Terminal Histone Modifications by the BRPF1 Bromodomain. ***J Mol Biol.*** 426(8): 1661-1676. PMCID: PMC3969779.

   b. Lubula MY, Eckenroth BE, Carlson S, Poplawski A, Chruszcz M, and **Glass KC** (2014) Structural insights into recognition of acetylated histone ligands by the BRPF1 bromodomain. ***FEBS Lett***. 588(21): 3844-54. PMCID: PMC4188086.

   c. Gay JC, Eckenroth BE, Evans CM, Langini C, Carlson S, Lloyd JT, Caflisch A, **Glass KC.** (2019) Dislulfide bridge formation influences ligand recognition by the ATAD2 bromodomain. ***Proteins*****,** Feb; 87(2): 157-167. PMCID: PMC6457126

   d. Lloyd JT, McLaughlin K, Lubula MY, Gay JC, Dest A, Gao C, Phillips M, Tonelli M, Cornilescu G, Marunde MR, Evans CM, Boyson SP, Carlson S, Keogh MC, Markley JL, Frietze S, and **Glass KC**. (2020) Structural insights into the recognition of mono- and di-acetylated histones by the ATAD2B bromodomain. ***J. Med Chem***. 2020 Nov 12;63(21):12799-12813. doi: 10.1021/acs.jmedchem.0c01178. Epub 2020 Oct 21. PMCID: PMC7884259.

4. **Combinatorial action of chromatin reader domains and histone modifications:** As a direct result of my research we have provided some insight into the higher-level regulation of gene expression that is modulated through histone modifications and their readers. The histone code is orders of magnitude more complex than the genetic code, and understanding this process is compounded by the presence and interaction of multiple chromatin reader domains within single enzymatic complexes. My research on the HBO1 and MOZ histone acetyltransferase complexes has highlighted how altering either the subunit composition of an enzymatic complex or the availability of particular combinations of histone modifications can dramatically affect the activity of chromatin remodelers, and epigenetic signaling programs within the cell. For example, we proposed a model describing how the cooperative action of multiple chromatin reader domains within the MOZ histone acetyltransferase regulates its acetylation activity in response to the epigenetic landscape.

a. Saksouk N, Avvakumov N*, **Champagne KS***, Hung T*, Doyon Y, Cayrou C, Paquet E, Ulla M, Landry AJ, Côté V, Yang XJ, Gozani O, Kutateladze TG and Côté J. (2009) HBO1 HAT complexes target chromatin throughout gene coding regions via multiple PHD finger interactions with histone H3 tail. ***Mol Cell****.* 33:257-265. PMCID: PMC2677731 *These authors contributed equally to the work.

b. Yuan CC, Matthews AG, Jin Y, Chen CF, Chapman BA, Ohsumi TK, **Glass KC**, Kutateladze TG, Borowsky ML, Struhl K, Oettinger MA. (2012) Histone H3R2 symmetric dimethylation and histone H3K4 trimethylation are tightly correlated in eukaryotic genomes. ***Cell Rep****.* Feb 23;1(2):83-90. PMCID: PMC3377377.

c. Carlson S and **Glass KC.** (2014) The MOZ Histone Acetyltransferase in Epigenetic Signaling and Disease. ***J Cell Physiol****.* Nov 229(11): 1571-4. PMCID: PMC4750494.

d. Obi JO, Lubula MY, Cornilescu G, Henrickson A, McGuire K, Evans CM, Phillips M, Boyson SP, Demeler B, Markley JL, **Glass KC**. The BRPF1 bromodomain is a molecular reader of di-acetyllysine. ***Curr Res Struct Biol.*** 2020;2:104-115. doi: 10.1016/j.crstbi.2020.05.001. Epub 2020 May 12. PMCID: PMC7861561.

Complete List of Published Work in MyBibliography
https://www.ncbi.nlm.nih.gov/myncbi/karen.glass.1/bibliography/public/

D. Research Support:

Ongoing Research Support

R01GM129338 Glass (PI)/Frietze (PI) 09/19/2018 - 08/31/2022
NIH/NIGMS
Deciphering the molecular mechanisms of histone code recognition by ATAD2/B
Goals: To characterize how cross-talk between adjacent histone modifications modulates acetyllysine recognition by the ATAD2/B bromodomains, outline the molecular mechanism of di-acetyllysine coordination and to connect the genome-wide associations of the ATAD2/B bromodomain-containing proteins to histone acetylation patterns and disease progression.
Role: Principle Investigator (multi-PI award)

P01CA240685 Stein (PI) 04/01/2021 – 03/31/2026
NIH/NCI
Epigenetic Control and Genome Organization
Goals of Project 2: To characterize the role of bromodomain-containing proteins as modulators of the endocrine response through epigenetic regulation of co-regulator pathways in ER+ breast cancer.
Role: Principle Investigator of Project 2 (multi-PI Project)

Research Support Completed During the Last Three Years

R15GM104865 Glass (PI) 02/01/2016 - 01/31/2019
NIH, NIGMS Academic Research Enhancement Award (AREA)
Mechanisms of chromatin binding and selection by family IV bromodomains
Goals: To establish the molecular mechanism of acetylated histone ligand selection by the family IV bromodomains
Role: Principle Investigator

Biographical Sketch

NAME: Phillips, Margaret

eRA COMMONS USER NAME (credential, e.g., agency login): PHILLIPSMAR

POSITION TITLE: Postdoctoral Fellow

EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE (if applicable)	COMPLETION DATE MM/YYYY	FIELD OF STUDY
University of Lucknow, Lucknow, India	BS	11/2004	Biology
University of Lucknow, Lucknow, India	MS	07/2007	Inorganic Chemistry
University of Lucknow, Lucknow, India	MPHIL	02/2010	Magnetic Resonance (MRI & MRS)
Nanyang Technological University, Singapore	PhD	07/2016	Biological Sciences
Nanyang Technological University, Singapore	Postdoctoral	06/2017 – 06/2019	NMR spectroscopy
Albany College of Pharmacy and Health Sciences (ACPHS), Colchester, VT, USA	Postdoctoral	06/2019 - present	Deciphering the molecular mechanisms of histone code recognition by ATAD2/B
2020 NMRFAM Virtual Workshop, University of Wisconsin-Madison	Training Course	06/2020	Introduction to Protein Structure Determination
11th Annual SIBYLS BioSAXS workshop 2020, Advanced Light Source, Berkeley, CA	Training Course	08/2020	Macromolecular Structural Biology
BioCAT Workshop: Everything BioSAXS 7, Getting Started in Biological Small Angle X-ray Solution Scattering (SAXS)	Training Course	03/2021	Macromolecular Structural Biology

A. Personal Statement

My long-term research focus is to use structural biology techniques to characterize the molecular mechanisms driving diverse protein functions. My academic and research experience has provided me excellent training in molecular biology, biochemistry, and various structural biology techniques. During my Ph.D. training, I worked under the supervision of Dr. Konstantin Pervushin and focused on using solution-state Nuclear Magnetic Resonance Spectroscopy for the structural characterization of membrane proteins – human Stromal Interaction molecule 1 precursor (hSTIM1), human Presenilin enhancer -2 (hPEN2), and *E.coli* water channel Aquaporin Z (AqpZ). I continued my postdoctoral training with Dr. Pervushin to gain additional experience in solid-state NMR spectroscopy and also received training in Transmission Electron Microscopy to obtain structural information of large proteins or protein complexes. My training in solid-state NMR data analysis, allowed me to characterize the binding of a small molecule inhibitor to the Aquaporin Z water channel. I collaborated with several labs within Singapore where my NMR data acquisition and analysis expertise were used to characterize the structure and function of various proteins and peptides such as Lipocalin-type prostaglandin D synthase (LPGDS) and peptides derived from squid sucker ring teeth as well as small peptides forming hydrogels. I became proficient in visualizing samples with negative staining techniques and characterized synthetic amyloid-beta fibrils as well fibrils derived from brain organoids, using negative stain imaging. During my second postdoctoral training, I had the opportunity to work with Dr. Karen C. Glass where I utilized my NMR expertise to help characterize the acetylated histones binding site on ATAD2/B and BRPF1

bromodomains. I have also learned to grow good quality crystals for X-ray crystallographic studies, and how to solve the 3D X-ray structure of these bromodomain-histone complexes using molecular replacement. I want to continue to build on my previous structural biology experiences by learning to collect and analyze Cryo-EM data. With the recent advances in Cryo-EM technology, it is now possible to get sub-atomic resolution of large multimeric complexes. My experience in Cryo-EM will thus enable me to take on more challenging projects which are too big for solution NMR and not easy to crystallize for X-ray studies. The conceptual and technical training in complementary techniques like NMR, X-ray, and Cryo-EM will enable me to achieve my goal of working towards a comprehensive understanding of protein function in various pathways and human disease progression.

1. Lloyd JT, McLaughlin K, Lubula MY, Gay JC, Dest A, Gao C, **Phillips M**, Tonelli M, Cornilescu G, Marunde MR, Evans CM, Boyson SP, Carlson S, Keogh MC, Markley JL, Frietze S, Glass KC. Structural Insights into the Recognition of Mono- and Diacetylated Histones by the ATAD2B Bromodomain. J Med Chem. 2020 Nov 12;63(21):12799-12813. PubMed Central PMCID: PMC7884259.
2. Alić I, Goh PA, Murray A, Portelius E, Gkanatsiou E, Gough G, Mok KY, Koschut D, Brunmeir R, Yeap YJ, O'Brien NL, Groet J, Shao X, Havlicek S, Dunn NR, Kvartsberg H, Brinkmalm G, Hithersay R, Startin C, Hamburg S, **Phillips M**, Pervushin K, Turmaine M, Wallon D, Rovelet-Lecrux A, Soininen H, Volpi E, Martin JE, Foo JN, Becker DL, Rostagno A, Ghiso J, Krsnik Ž, Šimić G, Kostović I, Mitrečić D, Francis PT, Blennow K, Strydom A, Hardy J, Zetterberg H, Nižetić D. Patient-specific Alzheimer-like pathology in trisomy 21 cerebral organoids reveals BACE2 as a gene dose-sensitive AD suppressor in human brain. Mol Psychiatry. 2020 Jul 10; PubMed PMID: 32647257.
3. Kannaian B, Sharma B, **Phillips M**, Chowdhury A, Manimekalai MSS, Adav SS, Ng JTY, Kumar A, Lim S, Mu Y, Sze SK, Grüber G, Pervushin K. Abundant neuroprotective chaperone Lipocalin-type prostaglandin D synthase (L-PGDS) disassembles the Amyloid-β fibrils. Sci Rep. 2019 Aug 29;9(1):12579. PubMed Central PMCID: PMC6715741.
4. **Phillips M**, To J, Yamazaki T, Nagashima T, Torres J, Pervushin K. Binding of a small molecule water channel inhibitor to aquaporin Z examined by solid-state MAS NMR. J Biomol NMR. 2018 Jun;71(2):91-100. PubMed PMID: 29916035.

B. Positions and Honors

Positions and Employment

2006 - 2007	Guest Lecturer, Isabella Thoburn College, Lucknow
2009 - 2009	Junior research fellow, Centre of Biomedical Magnetic Resonance, Lucknow
2010 - 2011	Research Associate , Nanyang Technological University, Singapore
2017 - 2019	Postdoctoral Fellow, Nanyang Technological University, Singapore
2019 - present	Postdoctoral Fellow, Albany College of Pharmacy and Health Sciences, Colchester, VT, USA

Other Experience and Professional Memberships

- Member of the American Society for Biochemistry and Molecular Biology (ASBMB)

Honors

2003 - 2004	Received Margaret Wallace Scholarship for Science student with first division marks and best participation in college activities, Isabella Thoburn College
2005 - 2006	Secured First Position in Masters in Science, University of Lucknow
2009	Awarded Junior Research fellowship, Centre of Biomedical Magnetic Resonance, India
2011 - 2016	Conferred Doctor of Philosophy, Nanyang Technological University
2014	Successfully completed the University teaching for Teaching Assistants, Nanyang Technological University

C. Contribution to Science

Early Career: During my M. Phil. course, I completed my final year project in the lab of Prof. RV Hosur at the Tata Institute of Fundamental Research in Mumbai, India. Over the period of three months, I spent in this lab, I gained an appreciation for research done in biological sciences. My project involved structural characterization of the HIV-1 protease mutant D25N protein. The mutation was done to remove a negative charge from the active site of the HIV-1 protease, which resulted in two slow-exchanging conformations at the N-terminus of the protease. My aim was to assist the Ph.D. student, Mr. Rout, in protease purification and sample preparation for acquiring NMR data. I also assisted in completing the backbone assignment of the mutant D25N during my three months project. Our findings on the subtle differences in the mutant and wild-type conformations were important to understand the efficacy of the protease function. This project allowed me greater insight into how biological labs work and helped me develop an aptitude for biological research.

a. Rout MK, Reddy JG, **Phillips M**, Hosur RV. Single point mutation induced alterations in the equilibrium structural transitions on the folding landscape of HIV-1 protease. J Biomol Struct Dyn. 2013;31(7):684-93. PubMed PMID: 22909351.

Graduate Career: I received my Ph.D. in structural biology from Nanyang Technological University, Singapore, where I worked on "The use of nuclear magnetic resonance in study of structurally dynamic membrane proteins such STIM1, PEN-2 and AqpZ. My previous degree in magnetic resonance provided me the necessary background to pursue a Ph.D. in NMR spectroscopy. Working with Dr. Konstantin Pervushin, a pioneer in the field of NMR, gave me an opportunity to study the technique in detail and gain expertise in how NMR can be successfully used to answer many structural biology questions while allowing proteins to remain in their biologically relevant environment. While working on the STIM1 collaboration with Dr. Said Eshaghi, I optimized the expression and purification of various constructs of full length human STIM1 protein. Stromal Interaction Molecule 1 (STIM1), an ER membrane protein, plays an important role in mediating calcium ion influx following calcium depletion. It was known to interact with the ORAI1 channel but no detailed information was available on how these proteins interact. I worked with STIM1 constructs that contained the canonical binding region to ORAI1 along with a transmembrane domain that anchors the STIM1 to the ER membrane. I studied the thermal stability and overall global fold of several of these constructs using Circular Dichroism, Thermoflour assay and solution NMR. To characterize calcium binding property and functional activity of these constructs I used solution-state heteronuclear NMR experiments. My second project, Presenilin Enhancer -2 (PEN2), a 100 amino-acid membrane protein, is an important component of the multimeric γ-secretase complex and is responsible for the functional activity of the whole complex. At the start of my graduate studies, there was no known structure for PEN2. Thus the main emphasis of my project involved structural characterization of this membrane protein using solution NMR. Using various NMR techniques such as Paramagnetic Relaxation experiments and hydrogen-deuterium exchange studies, I was able to identify the global fold of the elusive membrane protein. During my final year of Ph.D., I also learned how to analyze solid-state NMR data while working on the backbone assignment of the *E.coli* water channel Aquaporin Z membrane protein. This bacterial membrane protein served as a model to study and understand the functioning of the human aquaporins that function as important water channel regulators. This project was a collaboration with Dr. Yamazaki and Dr. Nagashima from the solid-state NMR facility in Riken, Japan, where the data was acquired and sent to me which I then analyzed to characterize the binding of small molecule inhibitor to AqpZ. During my 4 years of Ph.D. training, I was actively involved in several other small collaborations with labs in my Nanyang Technological University, Singapore where my NMR knowledge allowed me to characterize small peptides and molecules. Overall, my Ph.D. studies helped me understand and appreciate the process of scientific questioning, and how these questions can be answered by employing various biological techniques. I was also exposed to new ideas, techniques and gained more experience in designing and troubleshooting my experiments. All these experiences were crucial in building my passion for research and science.

a. How J, Zhang A, **Phillips M**, Reynaud A, Lu S, Pan L, Ho H, Yau Y, Guskov A, Pervushin K, Shochat S, Eshaghi S. Comprehensive Analysis and Identification of the Human STIM1 Domains for Structural and Functional Studies. PLoS ONE. 2013; 8(1):e53979-. Available from: https://dx.plos.org/10.1371/journal.pone.0053979 DOI: 10.1371/journal.pone.0053979

b. **Phillips M**, To J, Yamazaki T, Nagashima T, Torres J, Pervushin K. Binding of a small molecule water channel inhibitor to aquaporin Z examined by solid-state MAS NMR. Journal of Biomolecular NMR. 2018; 71(2):91-100. Available from: http://link.springer.com/10.1007/s10858-018-0195-0 DOI: 10.1007/s10858-018-0195-0
c. Hiew SH, Guerette PA, Zvarec OJ, **Phillips M**, Zhou F, Su H, Pervushin K, Orner BP, Miserez A. Modular peptides from the thermoplastic squid sucker ring teeth form amyloid-like cross-β supramolecular networks. Acta Biomater. 2016 Dec;46:41-54. PubMed PMID: 27693688.

Postdoctoral career: My first Postdoc training was under Dr. Konstantin Pervushin, Singapore. During this time, I learned how to record and analyze the solid-state NMR experiments and also trained in negative stain image acquisition. My training was useful in identifying the presence of fibrillar amyloid deposits in brain organoids derived from Down's syndrome patients, caused by trisomy 21, by using transmission electron microscopy. I also worked on identifying and characterizing synthetic amyloid β fibrils by TEM. This was very useful in understanding how the neuroprotective chaperone, lipocalin-type prostaglandin D synthase (LPGDS) which is the second most abundant chaperone in the cerebral-spinal fluid, can also dissemble the amyloid fibrils. During my postdoctoral training I also got the opportunity to mentor a Final Year Project student and together we worked on how Anticholinergic drugs interfere with the neuroprotective chaperone activity of LPGDS. These anticholinergic drugs have previously been linked to increase in Alzheimer's disease. Our findings demonstrated how binding to these small drug molecules results in a complex that shows decreased neuroprotective properties.

My second postdoctoral training under Dr. Karen C. Glass, USA, allowed me to use my NMR expertise to work on the structural characterization of bromodomain-histone complexes. Bromodomain proteins are known chromatin readers and have been known to play an important role in gene regulation and cellular proliferation and hence several cancers. In Glass lab we focus on how these bromodomains recognize the post-translational modifications on the histone proteins. With the help of solution NMR, we successfully characterized the acetyllysine binding pocket which highlights residue specific information that can assist in designing small molecule inhibitors to regulate bromodomain activity in-vivo. I also gained experience in setting up crystal screens and analyzing X-ray diffraction data for calculating 3D structure using molecular replacement which further informs on how the bromodomain residues are involved in histone interactions.

a. Alić I, Goh PA, Murray A, Portelius E, Gkanatsiou E, Gough G, Mok KY, Koschut D, Brunmeir R, Yeap YJ, O'Brien NL, Groet J, Shao X, Havlicek S, Dunn NR, Kvartsberg H, Brinkmalm G, Hithersay R, Startin C, Hamburg S, **Phillips M**, Pervushin K, Turmaine M, Wallon D, Rovelet-Lecrux A, Soininen H, Volpi E, Martin JE, Foo JN, Becker DL, Rostagno A, Ghiso J, Krsnik Ž, Šimić G, Kostović I, Mitrečić D, Francis PT, Blennow K, Strydom A, Hardy J, Zetterberg H, Nižetić D. Patient-specific Alzheimer-like pathology in trisomy 21 cerebral organoids reveals BACE2 as a gene dose-sensitive AD suppressor in human brain. Mol Psychiatry. 2020 Jul 10; PubMed PMID: 32647257.
b. Kannaian B, Sharma B, **Phillips M**, Chowdhury A, Manimekalai MSS, Adav SS, Ng JTY, Kumar A, Lim S, Mu Y, Sze SK, Grüber G, Pervushin K. Abundant neuroprotective chaperone Lipocalin-type prostaglandin D synthase (L-PGDS) disassembles the Amyloid-β fibrils. Sci Rep. 2019 Aug 29;9(1):12579. PubMed Central PMCID: PMC6715741.
c. Yi, KLJ, **Phillips, M,** Pervushin, K. Anticholinergic Drugs Interact with Neuroprotective Chaperone L-PGDS and Modulate Cytotoxicity of Aβ Amyloids. Front Pharmacol. 2020 Jun 11;11:862. doi: 10.3389/fphar.2020.00862.
d. Obi J, Lubula M, Cornilescu G, Henrickson A, McGuire K, Evans C, **Phillips M**, Boyson S, Demeler B, Markley J, Glass K. The BRPF1 bromodomain is a molecular reader of di-acetyllysine. Current Research in Structural Biology. 2020; 2:104-115. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2665928X20300106 DOI: 10.1016/j.crstbi.2020.05.001
e. Lloyd JT, McLaughlin K, Lubula MY, Gay JC, Dest A, Gao C, **Phillips M**, Tonelli M, Cornilescu G, Marunde MR, Evans CM, Boyson SP, Carlson S, Keogh MC, Markley JL, Frietze S, Glass KC. Structural Insights into the Recognition of Mono- and Diacetylated Histones by the ATAD2B Bromodomain. J Med Chem. 2020 Nov 12;63(21):12799-12813. PubMed Central PMCID: PMC7884259.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1Hy0sp8QnCHw0c/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

Scholastic Performance

YEAR	COURSE TITLE	GRADE
UNIVERSITY OF LUCKNOW		
2004	Chemistry	206/300
2004	Botany	207/300
UNIVERSITY OF LUCKNOW		
2006	Inorganic Chemistry	927/1200
UNIVERSITY OF LUCKNOW		
2009	Magnetic Resonance and Magnetic Imaging	493/600
NANYANG TECHNOLOGICAL UNIVERSITY		
2016	Doctor of Philosophy	4.0

PHD: Cumulative grade point average is the grade point average of all courses. Grade point 4.00 corresponds to B+. Passing cumulative grade point is 3.0. BS,MS and MPhil: Marks obtained over Maximum marks for each degree obtained. The passing percentage is 40%.