Curriculum Vitae **Kathleen Mulvaney**

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EDUCATION

UNIVERSITY OF NORTH CAROLINA CHAPEL HILL PhD in Cell Biology

Dissertation: Proteomic dissection of KEAP1/NRF2 signaling identifies novel pathway interactors

- Courses in Cell Biology, Biochemistry, Molecular Biology, Cancer Biology and Immunology
- Workshops in Critical Thinking, Grant Writing and Presenting Scientific Research

UNIVERSITY OF ROCHESTER

Bachelors of Science in Biology

Concentration in Molecular Genetics with Distinction in Research

Advanced coursework in Molecular Biology, Genetics, Biochemistry, Tumor Immunology, Microbiology, Cell Biology, Cognitive Science and Neuroscience

RESEARCH EXPERIENCE

THE BROAD INSTITUTE: DANA FARBER CANCER INST. Postdoctoral Fellow with Dr. William (Bill) Sellers

- Research focus on targeting protein-protein interactions for therapeutic development in cancer •
- Therapeutically targeting PRMT5 on a novel binding interface in pancreatic cancer
- Led a productive team of 2-3 research associates funded by NIH and Deerfield Management support •
- Collaborated with the Center for Development of Therapeutics to complete drug discovery project •
- Culminated in two research publications and one patent •

UNIVERSITY OF NORTH CAROLINA CHAPEL HILL Postdoctoral Fellow with Dr. Ben Major

Completed screen and manuscript identifying NRF2 interacting proteins and transcriptional regulators •

UNIVERSITY OF NORTH CAROLINA CHAPEL HILL

Graduate Student with Dr. Ben Major

- Research focus on the KEAP1-NRF2 signaling pathway in cancer •
- Described a function for KEAP1 in cell cycle regulation through ubiquitylation of MCM3
- Proteomic screening identified novel NRF2 interacting proteins and transcriptional regulators
- Culminated in successful defense of PhD, a first-author paper, a first-author review and three additional manuscripts

DANA FARBER CANCER INSTITUTE, HARVARD UNIVERSITY **Research Assistant with Dr. Alan Engelman**

Performed ChIP-Sequencing project to determine lens epithelial derived growth factor, LEDGF, • binding sites and thereby identify preferential HIV-1 integration sites throughout the genome

UNIVERSITY OF ROCHESTER Lab Assistant with Dr. Shawn Murphy

ROCHESTER, NY February 2007 - May 2009

ROCHESTER, NY May 2010

CHAPEL HILL, NC

December 2016

CHAPEL HILL. NC December 2016-May 2017

CHAPEL HILL. NC

Spring 2011-December 2017

BOSTON, MA

Summer 2009

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CAMBRIDGE. MA

June 2017-Present

- Research Focus on Diffuse Large B-Cell Lymphoma and expression of MHC Class II and CIITA with the underlying goal of identifying the association between expression levels and patients' immunological responses to DLBCL tumors
- Culminated in writing and successful defense of senior thesis and two co-authored manuscripts

PUBLICATIONS

- <u>Mulvaney, KM</u>; Blomquist, C; Acharya, N; Li, R; Ranaghan, MJ; O'Keefe, M; Rodriguez, DJ; Young, MJ; Kesar, D; Pal, D; Stokes, M; Nelson, AJ; Jain, SS; Yang, A; Mullin-Bernstein, Z; Columbus, J; Bozal, FK; Skepner, A; Raymond, D; ... Sellers, WR. Molecular basis for substrate recruitment to the PRMT5 methylosome. *Molecular Cell*. 2021, 81(17)17, P3481-3495.
- McKinney, DC; McMillan, BJ; Ranaghan, MJ; Moroco, JA; Brousseau, M; Mullin-Bernstein, Z; O'Keefe, M; McCarren, P; Mesleh, M; <u>Mulvaney, KM</u>; Robinson, F; Singh, R; Bajrami, B; Wagner, FF; Hilgraf, R; Drysdale, MJ; Campbell, AJ; Skepner, A; Timm, DE; Porter, D; Kaushik, VK; Sellers, WR; Ianari, A. Discovery of a First-in-Class Inhibitor of the PRMT5–Substrate Adaptor Interaction. *Journal of Medicinal Chemistry*. 2021, 64 (15), 11148-11168.
- Song, S; Nguyen, V; Schrank, T; <u>Mulvaney, KM</u>; Walter, V.; Wei, D.; Orvis, T.; Desai, N.; Zhang, J.; Hayes, DN; Zheng, Y.; Major, MB; Weissman, B. Loss of SWI/SNF chromatin remodeling alters NRF2 signaling in non-small cell lung carcinoma. *Mol Cancer Res.* 2020, Dec; 18(12):1777-1788.
- Bowman BM; Montgomery SA Schrank TP, Simon JM, Ptacek TS, Tamir TY, <u>Mulvaney KM</u>, Weir SJ, Nguyen TT, Murphy RM, Makowski L, Hayes DN, Chen XL, Randell SH, Weissman BE, Major MB. A conditional mouse expressing an activating mutation in NRF2 displays hyperplasia of the upper gastrointestinal tract and decreased white adipose tissue. *J Pathol.* 2020 Oct;252(2):125-137.
- Mulvaney, KM.; Matson, J.; Siesser, P.; Tamir, TY; Goldfarb, D.; Jacobs, T.; Cloer, EW; Cook, JG; Major, MB. Identification and Characterization of MCM3 as a KEAP1 Substrate. *Journal of Biological Chemistry*, 2016 Nov 4; 291(45): 23719–23733.
- 6. Tamir, TY*; <u>Mulvaney, KM*</u>; Major, MB. Dissecting the Keap1/Nrf2 pathway through proteomics. *Current Opinion in Toxicology*, (*equal contribution) 2016, 1:118-24.
- Guntas, G; Lewis, S; <u>Mulvaney, KM</u>; Cloer, E; Tripathy, A; Lane, T; Major, MB; Kuhlman, B. Engineering a genetically encoded competitive inhibitor of the KEAP1-NRF2 interaction via structure- based design and phage display. *Protein Eng Des Sel.* 2016 Jan;29(1):1-9.
- Hast, BE; Goldfarb D*; <u>Mulvaney KM*</u>; Hast MA; Siesser PF; Yan F; Hayes DN; Major MB. Proteomic analysis of ubiquitin ligase KEAP1 reveals associated proteins that inhibit NRF2 ubiquitination. *Cancer Research*. 2013 1;73(7):2199-210. (*equal contribution)
- Cycon, KA; <u>Mulvaney, KM</u>; Rimsza, LM; Persky, D.; Murphy, SP. Histone deacetylases (HDACs) contribute to the silencing of CIITA expression in DB diffuse large B cell lymphoma. *Immunology*. 2013 Oct; 140(2): 259–272.
- Bushway, M.; Cycon, KA; <u>Mulvaney, KM</u>; Murphy, SP. Coordinate loss of MHC class II expression in the diffuse large B cell lymphoma cell line OCI-Ly2 is due to a novel mutation in RFX-AP. *Immunogenetics*. 2010, 62(2):109-16.

PUBLICATIONS IN PROGRESS

- 1. <u>Mulvaney, KM</u>; Bozal, FK; Sellers, WR. Monitoring and disrupting cellular PRMT5-substrate adaptor complex formation in in-tact and permeabilized cells using a split luciferase complementation assay. *STAR Protocols, Cell Press.* Manuscript in preparation.
- Pal, D; Rodriguez, D; Chang, L; Robinson, F; Potter, D; Kesar, D; Li, R; Van Tienen, L; <u>Mulvaney</u>, <u>KM</u>; Jung, N; Jain, S; Park, J; Letai, A; Sellers, WR. WSB2 is a novel regulator of the cellular

apoptotic pathway and a therapeutic target in melanoma. Submitted to Cancer Cell.

PROJECTS IN PROGRESS

- 1. Identifying mechanisms of resistance and sensitizers to PRMT5 chemical inhibitors using single and digenic CRISPr KO screens.
- 2. In collaboration with Dr. Eric Fischer: Structurally resolving a full-length methylosome-substratesubstrate adaptor complex by Cryo-EM.

PATENTS

1. Arthur Campbell, Martin Drysdale, Robert Hilgraf, Alessandra Ianari, Patrick McCarren, David McKinney, Brian McMillan, Kathleen Mulvaney, Dale Porter, William Sellers, Ritu Singh, Florence Wagner. Co-inventor, PCT Application Serial No. PCT/US2021/045016, filed on August 6, 2021 and entitled, "Substrate Adaptor Inhibitors of PRMT5 and Uses Thereof". (inventors listed alphabetically)

AWARDS

•	NIH F32 Ruth L. Kirschstein Postdoctoral Individual National Research Service Award	(2018-2021)
•	NIH LRP Award	(2019-2021)
•	Sigma Xi Research Society Graduate Student Travel Award	(2015)
•	National Science Foundation Graduate Research Fellowship Honorable Mention	(2011, 2012)
•	Degree with Distinction in Research: an honor awarded by the University of Rochester	(2009)
•	National Science Foundation David T. Kearns Scholar	(2008-2010)
•	Take Five Scholar: Awarded tuition-free fifth year by the University of Rochester to study "Influences	
	on Cognitive and Personality Development"	(2009-2010)
•	Academic Competitiveness Grant awarded by New York State	(2007-2008)
•	International Baccalaureate Scholar awarded as a four-year merit scholarship	(2005-2009)

PRESENTATIONS

NATIONAL MEETINGS			
FASEB Biological Methylation Conference	June 2022, Accepted Abstract-Talk		
AACR Annual Meeting April 2022, Accepted Abstract-Poster			
AACR Annual Meeting	April 2016		
 Presented "KEAP1 ubiquitinates MCM3 to regulate cell cycle in cancer" poster 			
FASEB Ubiquitin ConferenceJune 2014			
• Presented "KEAP1 ubiquitinates MCM3" poster to the ubiquitin-proteasome signaling community			
DANA FARBER HARVARD CANCER CENTER			
Mass. General Hospital Postdoc Association Invited Seminar	February 2022		
• Presented "Drugging Enzymes in Cancer" to a general audie	nce, invited seminar		
Ludwig Meeting Invited Seminar	July 2021		
• Presented "Resolving substrate recruitment to the PRMT5 methylosome" invited seminar			
Molecular and Cellular Oncology Retreat	June 2019		
• Awarded Best Poster Presentation: "PRMT5-substrate adaptor interface as a novel therapeutic target			
in MTAP null tumors"			
BROAD INSTITUTE			
Lunch and Learn July 2019			

Co-led department-wide invited chalk talk: "Opportunities and challenges in following up cancer • dependencies: lessons learned from PRMT5 and NXT1"

UNIVERSITY OF NORTH CAROLINA CHAPEL HILL

University Research Day

Awarded Best Oral Presentation

IMSD Symposium

Awarded Best Oral Presentation

UNIVERSITY OF ROCHESTER

Office of Admissions

Invited to present regionally to prospective students on undergraduate research opportunities •

TEACHING EXPERIENCE

HARVARD UNIVERSITY, HARVARD EXTENSION SCHOOL, CAMBRIDGE, MA **BIOS E-30 Epigenetics & Gene Regulation Teaching Assistant and Guest Lecturer** Fall 2020, Fall 2021

- Led weekly independent recitation and study sections, guided and graded the writing assignments
- Teaching 2 lectures per seminar on cancer epigenetics (2021)

BIOS E-16 Cell Biology Teaching Assistant

- Led weekly independent recitation and study sections
- Guided and graded the writing assignments, problem sets, and exams

BROAD INSTITUTE, CAMBRIDGE, MA

Graduate Student Mentoring

• Mentoring Harvard BBS students rotating in the lab in critical thinking and scientific research

Research Associate Mentoring

• Mentoring and promoting the career development of three post-undergraduate researchers in the lab.

UNIVERSITY OF NORTH CAROLINA, CHAPEL HILL, NC

Science-at-Hand

Give monthly scientific demonstrations and discuss careers in science with high school students. •

Undergraduate Mentoring

• Mentoring two undergraduate researchers on research projects for credit in the Major Lab.

First Year Group

Peer mentor to first year students, advise on lab rotations and giving scientific presentations.

North Carolina DNA Day

• Taught high school students about pharmacogenomics and encouraged exploring careers in science.

UNIVERSITY OF ROCHESTER, ROCHESTER, NY

Upward Bound Tutoring

National initiative to assist high school students from disadvantaged backgrounds enter college

Refugee Tutoring

Fall 2009-Spring 2010

Fall 2008-Spring 2011

September 2017-Present

Spring 2019; Spring 2021

June 2017-Present

March 2015

November 2014

December 2008

October 2014-May 2017

January 2014- May 2017

Fall 2014

April 2011; April 2013



• Program to assist high school, middle school refugees from Turkey and Somalia relocated to the US

Lab Teaching Assistant, Department of Chemistry

Fall 2006

• Prepared laboratory set-up for general chemistry students and reviewed and graded lab reports.

LABORATORY TECHNIQUES

PROTEOMICS: Experience with purification of protein complexes for identification by mass spectrometry (affinity, immunoprecipitation and BioID), isolation and detection of whole cell and targeted post-translational modifications (phosphorylation, ubiquitylation, methylation) by mass spectrometry, and analysis and visualization of mass spectrometry data (MaxQuant, Proteome Discoverer, Skyline, Spotlite, Cytoscape).

MOLECULAR BIOLOGY & BIOCHEMISTRY: Experience with mammalian cell culture (primary and immortalized), RNA and DNA isolation, qPCR, RNA-seq, genetic manipulation including CRISPr, cloning and site-directed mutagenesis, flow cytometry, chromatin immunoprecipitation, luciferase reporter assays, drug treatments and viability and proliferation assays, protein expression and purification, Western blotting, fixed and live-cell light and fluorescence microscopy, proximity ligation assays, mouse handling, MEF line derivation, subcutaneous xenografts, recombinant protein purification, size exclusion chromatography, and cellular and *in vitro* binding and ubiquitylation assays.

GENOMICS, SCREENING AND NEXT-GEN SEQUENCING: Experience with single and digenic CRISPr knockout screens, small molecule screening, library generation and Illumina sequencing.

PROFESSIONAL MEMBERSHIPS

American Association for Cancer Research (AACR) (2016-present) American Association for the Advancement of Science (AAAS) (2015-present)

JOURNAL REVIEWER

Molecular Cancer Research (2019-present)