Melinda M. Diver, Ph.D.

Memorial Sloan Kettering Cancer Center
Assistant Member, Structural Biology

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POSITIONS

Memorial Sloan Kettering Cancer Center 2021 – present
Assistant Member in the Structural Biology Program

EDUCATION

University of California, San Francisco 2016 – 2021
Postdoctoral Research Fellow in the Department of Physiology
Mentor: David Julius, Ph.D.

Weill Cornell Graduate School of Medical Sciences 2007 – 2014
Ph.D. in Biochemistry and Structural Biology (degree conferred January 2015)
Mentor: Stephen Long, Ph.D. (Memorial Sloan Kettering Cancer Center)

University of British Columbia 2002 – 2007
B.Sc. Honors in Biochemistry (Co-operative Education Program)

PUBLICATIONS

Diver, M.M., Cheng, Y. & Julius, D. Structural insights into TRPM8 inhibition and desensitization. *Science.* 365, 1434-1440 (2019).

Diver, M.M., Pedi, L., Koide, A., Koide, S. & Long, S.B. Atomic structure of the eukaryotic intramembrane RAS methyltransferase ICMT. *Nature* 553, 526-529 (2018).

Diver, M.M. & Long, S.B. Mutational analysis of the integral membrane methyltransferase isoprenylcysteine carboxyl methyltransferase (ICMT) reveals potential substrate binding sites. *J. Biol. Chem.* 289, 26007-26020 (2014).

Hou, X., Pedi, L., **Diver, M.M.** & Long, S.B. Crystal structure of the calcium release-activated calcium channel Orai. *Science* 338, 1308-1313 (2012).

Garrey, S.M., Blech, M., Riffel, J.L., Hankins, J.S., Stickney, L.M., **Diver, M.**, Roger Hsu Y., Kunanithy, V. & Mackie, G.A. Substrate binding and active site residues in RNase E and G: the role of the 5'-sensor. *J. Biol. Chem.* 284, 31843-31850 (2009).

Keppetipola, N., Jain, R., Meineke, B., **Diver, M.** & Shuman, S. Structure-activity relationships in *Kluyveromyces lactis* γ–toxin, a eukaryal tRNA anticodon nuclease. *RNA* 15, 1036-1044 (2009).

Accepted: **Diver, M.M.**, Lin King, J.V., Julius, D. & Cheng, Y. Sensory TRP channels in three dimensions. Invited review to be published in *Annu. Rev. Biochem.* 91 (2022).

FUNDING

2021 – 2026 Josie Robertson Investigator, Memorial Sloan Kettering Cancer Center (5 years)
Role: PI, Amount: $1,500,000

2019 – 2024 NIH Pathway to Independence Award (K99/R00), National Center for Complementary and Integrative Health (NCCIH) (5 years)
Mechanistic studies of the menthol receptor TRPM8: A novel target for analgesic drugs
Role: PI, Amount: $242,460 (K99) + $747,000 (R00)

2017 – 2019 A. P. Giannini Postdoctoral Fellowship and Career Award, A. P. Giannini (3 years)
Elucidating the structural basis of cold sensation
Role: PI, Amount: $156,000

2017 NIH Ruth L. Kirchstein Postdoctoral Individual National Research Service Award (F32), NINDS (3 years - Declined upon accepting A. P. Giannini Postdoctoral Fellowship and Career Award)
Elucidating the structural basis of cold sensation
Role: PI, Amount: $178,590

2017 American Heart Association Postdoctoral Fellowship, American Heart Association (2 Years - Declined upon accepting A. P. Giannini Postdoctoral Fellowship and Career Award)
Elucidating the structural basis of cold sensation
Role: PI, Amount: $106,532

2012 – 2013 American Heart Association Pre-doctoral Fellowship, American Heart Association (2 Years)
Three-dimensional structure and mechanism of iosprenylcysteine caryoxymethyltransferase
Role: PI, Amount: $44,000

2010 – 2011 Dorris J. Hutchinson Fellowship, Memorial Sloan Kettering Cancer Center (1 Year)
Atomic structure and mechanism of the cancer drug target ICMT
Role: PI, Amount: Full Stipend + $2,000

2007 DAAD RISE professional Scholarship, German Academic Exchange Service (2 Months)
Role: PI, Amount: Full Stipend

2005 Undergraduate Student Research Award, Natural Science and Engineering Research Council of Canada (16-weeks)
Role: PI, Amount: Full Stipend

RESEARCH EXPERIENCE

Postdoctoral Research Fellow 04/2016 – 08/2021
University of California, San Francisco, Department of Physiology, San Francisco, CA, USA
Mentor: David Julius, Ph.D.
Close Collaborator: Yifan Cheng, Ph.D.
Project: Structural and mechanistic studies of the cold and menthol receptor TRPM8
Delineated molecular mechanisms of cation transport by the cold- and menthol-sensitive receptor, transient receptor potential melastatin 8 (TRPM8), using single-particle cryo-electron microscopy (cryo-EM) and electrophysiological studies, thereby revealing how this important somatosensory ion channel binds and responds to ligands and cellular regulatory factors.
Work published in *Science* (2019). Work funded through an A.P. Giannini postdoctoral fellowship and a NIH K99 transition award.

Postdoctoral Research Fellow 11/2014 – 03/2016
Memorial Sloan Kettering Cancer Center, Structural Biology Program, New York, NY, USA
Mentor: Stephen Long, Ph.D.
Project: Structural studies of the eukaryotic integral membrane methyltransferase ICMT
As a continuation of my doctoral research, determined the X-ray crystal structure of isoprenylcysteine carboxyl methyltransferase (ICMT), a promising therapeutic target for Ras-driven cancers, providing insight into how this intramembrane enzyme facilitates the access of reactants that have dramatically different physiochemical properties to a common active site while maintaining specificity for its diverse substrates.
Work published in *Nature* (2018).

Doctoral Training 3/2008 – 10/2014
Memorial Sloan Kettering Cancer Center, Structural Biology Program, New York, NY, USA
Mentor: Stephen Long, Ph.D.
Defense Chairperson: Minkui Luo, Ph.D.
Thesis Committee Members: Christopher Lima, Ph.D. and Stewart Shuman, M.D., Ph.D.
Dissertation: Structural and functional studies of the eukaryotic integral membrane methyltransferase ICMT
Made significant progress towards determining the X-ray crystal structure of ICMT through its purification, biochemically characterization, and initial crystallization. Large-scale scanning mutagenesis of ICMT led to the identification of amino acid residues critical for substrate binding and catalysis.
Work published in *J. Biol. Chem.* (2014). Work funded through Dorris J. Hutchinson and American Heart Association predoctoral fellowships.
Contributed to the X-ray structure determination of the calcium-release activated channel (CRAC), Orai, providing insight into its selective calcium permeation and gating.
Work published in *Science* (2012).

Rotation Student 1/2008 – 3/2008
Memorial Sloan Kettering Cancer Center, Molecular Biology Program, New York, NY, USA
Mentor: Stewart Shuman, M.D., Ph.D.

Characterized the enzymatic activity of the tRNA anticodon nuclease γ-toxin.
Work published in *RNA* (2009).

Rotation Student 9/2007 – 12/2007
Memorial Sloan Kettering Cancer Center, Molecular Biology Program, New York, NY, USA
Mentor: Kenneth Marians, Ph.D.
Studied the reactivation of stalled DNA replication forks using *in vitro* reconstitution.

DAAD RISE professional Intern 6/2007 – 7/2007
Bayer Technology Services, Leverkusen, Germany
Mentor: Christoph Methfessel, Ph.D.
Studied ion transport in small cell lung cancer cells (SCLCs) using automated patch-clamp.
Work funded through a DAAD RISE professional scholarship.

Honors Student Researcher 9/2006 – 4/2007
University of British Columbia, Department of Biochemistry and Molecular Biology, Vancouver, BC, Canada
Mentor: George Mackie, Ph.D.
Dissertation: The 5'-monophosphate sensor in Ribonuclease G
Uncovered which amino acid residues of the RNase E/G endoribonucleases contribute to substrate binding and catalysis.
Work published in *J. Biol. Chem.* (2009).

Co-op Student Researcher 1/2006 – 8/2006
Universität Halle-Wittenberg, Institut für Biochemie, Halle, Germany
Mentor: Elmar Wahle, Ph.D.
Investigated mRNA deadenylation using various biochemical approaches.

Co-op Student Researcher 9/2005 – 12/2005
James Hogg Research Centre at St. Paul's Hospital, Department of Medicine, Vancouver, BC, Canada
Mentors: Keith Walley, M.D. and James Russell, M.D.
Explored innate immunity genes associated with severe infection susceptibility in cardiac surgery and intensive care patients using genetic polymorphism studies.

Co-op Student Researcher 5/2005 – 8/2005
University of British Columbia, Department of Botany, Vancouver, BC, Canada
Mentor: Xin Li, Ph.D.
Screened for genes critical for signal transduction pathways of plant disease resistance.
Work funded through a Natural Science and Engineering Research Council of Canada undergraduate student fellowship.

MENTORING AND TEACHING EXPERIENCE

Research Mentor
Mentored numerous undergraduate and graduate student trainees, including members of underrepresented groups. Responsible for overseeing project design and management, teaching of laboratory techniques, and daily guidance. Aimed to foster independence.

Julius Lab, University of California, San Francisco, San Francisco, CA, USA

Adamo Mancino (PhD Candidate) 2020 – 2021
Current status: PhD Candidate at University of California, San Francisco
Moses Kwang Jin Chung (Undergraduate Summer Student) 2017
Current status: MD/PhD Candidate at Washington University School of Medicine in St. Louis

Long Lab, Memorial Sloan Kettering Cancer Center, New York, NY, USA
James Asciolla (PhD Candidate) 2013
Current status: PhD Candidate at Weill Cornell Graduate School of Medical Sciences
David Kerr, M.D. (Undergraduate Summer Student) 2013
Current status: Resident, Orthopeadic Surgery, Duke University School of Medicine
Johnathan Steinman, M.D., Ph.D. (MD-PhD Candidate) 2010
Current status: Resident, Pediatrics, Columbia University
Siddarth Venkatesh, Ph.D. (PhD Candidate) 2008
Current status: Instructor at Washington University School of Medicine in St. Louis

Leadership Training Program 2018
A. P. Giannini Foundation, Tiburon, CA, USA
Participated in a two-day retreat advising on key academic leadership skills, including how to collaborate effectively, contribute to problem solving, and maximize personal leadership strengths. Emphasis was placed on countering unconscious bias and creating a diverse and inclusive lab culture.

TRAIN-UP Introduction to Mentoring Program 2017
University of California, San Francisco, San Francisco, CA, USA
Completed an intensive 15-hour workshop series that teaches how to hire, teach, train, and supervise research trainees. Primary focuses were the mentoring of those who aren't like you, creating a supportive climate for everyone, and avoiding micro-inequities.

Teaching Assistant for Graduate Level Biochemistry 2008
Weill Cornell Graduate School of Medical Sciences, New York, NY, USA
Supported graduate student learning, including for those from underrepresented minority groups, by leading discussion sections after lectures, developing practice problems, and one-on-one tutoring.
Topics taught: Thermodynamics, Kinetics, Enzymology, and Protein Purification

RELATED PROFESSIONAL EXPERIENCE

Ad Hoc Reviewer 2020 – present
British Journal of Pharmacology
Engaged in the peer-review process by evaluating manuscripts within my area of expertise.

Communications Training Program 2017 – 2018
A. P. Giannini Foundation, San Francisco, CA, USA
Completed a series of virtual one-on-one meetings with a media expert aimed at improving fundamental communication skills. Culminated in the production and publication of a video disseminating my postdoctoral research to a broad audience.
Video link: www.youtube.com/watch?v=d1j2l43L7wk

Ad Hoc Co-reviewer 2016 – 2020
Cell, eLife, Nature, Proceedings of the National Academy of Sciences

Participated in assessing the validity and quality of manuscripts alongside my postdoctoral mentor Dr. David Julius.

Science Outreach Volunteer 2016
California Academy of Science, San Francisco, CA, USA
Designed and presented a public outreach program related to sensory biology for the Nightlife Series.

Poster Evaluator 2015
Vincent du Vigneaud Memorial Research Symposium, New York, NY, USA
Evaluated graduate student poster presentations and provided constructive feedback.

Postdoc/Faculty Forum 2014 – 2015
Memorial Sloan Kettering Cancer Center, New York, NY, USA
Attended a series of small group discussions led by faculty focused on setting-up and managing an inclusive academic lab.

Cold Spring Harbor Laboratory: X-ray Methods in Structural Biology 2009
Participated in an intensive laboratory/computational 16-day course focused on the theory and application of techniques used to determine X-ray crystallographic structures of macromolecules (competitive application process).

Let's Talk Science Volunteer 2004 – 2007
University of British Columbia, Vancouver, BC, Canada
Developed and delivered hands-on science activities for elementary and secondary students in the classroom and community to establish positive attitudes towards science within diverse audiences.

STEM Outreach Web Research and Development Coordinator 2004
Let's Talk Science, London, ON, Canada
Fostered the engagement of children, from a variety of backgrounds, in STEM through the compilation of free web resources for learners and educators. Made recommendations pertaining to science education and the impact of science outreach, with a focus on underrepresented minority groups, to the organization.

PRESENTATIONS

2021 *American Society for Biochemistry and Molecular Biology (ASBMB) Lipid Research Division Seminar Series, Virtual*
(Invited Speaker) Hot'n Spicy? Cool'n Minty? Lipid regulation of TRP channels

St. Jude Children's Research Hospital, Department of Structural Biology, Virtual
(Invited Speaker) Low temperature view of a cold sensor: structural insights into TRPM8 function and pharmacology

University of Pennsylvania, Department of Physiology, Virtual
(Invited Speaker) Low temperature view of a cold sensor: structural insights into TRPM8 function and pharmacology

Broad Institute's Next Generation in Biomedicine Symposium, Virtual
(Invited Speaker) Structural insights into the analgesic drug target TRPM8

2020 *Gordon Research Conference – Three Dimensional Electron Microscopy, Barcelona, Spain*
(Invited Speaker) Structural insights into the analgesic drug target TRPM8
(Cancelled due to the COVID-19 pandemic)

Bay Area CryoEM Meeting, Dublin, CA, USA
(Poster) Structural insights into the inhibition and desensitization of the cold receptor TRPM8

2019 *UCSF EM Supergroup, San Francisco, CA, USA*
(Invited Speaker) Structural insights into inhibition and desensitization of the cold and menthol receptor TRPM8

FASEB Conference – The Regulation and Function of Small GTPases, Olean, NY, USA
(Invited Speaker) Atomic structure of the eukaryotic intramembrane RAS methyltransferase ICMT

2018 *A. P. Giannini Postdoctoral Fellowship Colloquium, Stanford, CA, USA*
(Invited Speaker) Decoding the workings of our temperature sensors to relieve chronic pain

2015 *Hybrid Methods in Structural Biology Keystone Symposia, Lake Tahoe, CA, USA*
(Poster) Mutational analysis of the integral membrane methyltransferase ICMT reveals potential substrate binding sites

2014 *Weill Cornell Graduate School Thesis Defense, New York, NY, USA*
Structural and functional studies of the eukaryotic integral membrane methyltransferase ICMT

Vincent du Vigneaud Memorial Research Symposium, New York, NY, USA
(Invited Speaker) Mapping the substrate binding sites of the integral membrane methyltransferase ICMT by mutational analysis

Weill Cornell Structural Biology Discussion Group, New York, NY, USA
(Lecture) Mapping the substrate binding sites of the integral membrane methyltransferase ICMT by mutational analysis

Biophysical Society Annual Meeting, San Francisco, CA, USA
SRAA Poster Competition Winner
(Poster) Mapping the substrate binding sites of the integral membrane methyltransferase ICMT by mutational analysis

2013 *Weill Cornell BCMB Allied Program Retreat, New Platz, NY, USA*
(Poster) Mutational analysis of the integral membrane methyltransferase ICMT

Gordon Research Conference – Enzymes, Coenzymes & Metabolic Pathways, Waterville Valley, NH, USA
(Poster) Mutational analysis of the integral membrane methyltransferase ICMT

Vincent du Vigneaud Memorial Research Symposium, New York, NY, USA
(Poster) Mutational analysis of the integral membrane methyltransferase ICMT

Biophysical Society Annual Meeting, Philadelphia, PA, USA
(Poster) Mutational analysis of the integral membrane methyltransferase ICMT

Weill Cornell Structural Biology Discussion Group, New York, NY, USA
(Lecture) Crystallizing membrane proteins using the lipidic cubic phase (LCP)

2012 *Weill Cornell BCMB Allied Program Retreat, Skytop, PA, USA*
(Poster) Mutational analysis of the Ras drug target ICMT

Mid-Atlantic Macromolecular Crystallography Meeting, Charlottesville, VA, USA
(Poster) Mutational analysis of isoprenylcysteine carboxylmethyltransferase

Vincent du Vigneaud Memorial Research Symposium, New York, NY, USA
(Poster) Towards the three-dimensional structure and mechanism of the Ras drug target ICMT

Biophysical Society Annual Meeting, San Diego, CA, USA
(Poster) Mutational analysis of isoprenylcysteine carboxylmethyltransferase

2011 *Weill Cornell Structural Biology Discussion Group, New York, NY, USA*
(Lecture) Determining X-ray crystallographic structures of membrane proteins

Weill Cornell BCMB Allied Program Retreat, Skytop, PA, USA
(Invited Speaker) Towards the three-dimensional structure and mechanism of the Ras drug target ICMT

Weill Cornell BCMB Graduate Research Seminar, New York, NY, USA
Towards the atomic structure and mechanism of the Ras drug target ICMT

2010 *Weill Cornell BCMB Graduate Research Seminar, New York, NY, USA*
Atomic structure and mechanism of the cancer drug target ICMT

2007 *University of British Columbia Multidisciplinary Undergraduate Research Conference, Vancouver, BC, Canada*
(Poster) Gene regulation: exploring the phosphate sensor in *E. coli* Ribonuclease G

HONORS AND AWARDS

2020 Postdoc “Work-from-Home” Award, University of California, San Francisco

2014 Student Research Achievement Award, Biophysical Society

2014 Education Travel Award, Biophysical Society

2009 X-ray Methods in Structural Biology Course Stipend, Cold Spring Harbor Laboratory

2006 – 2007 Society of Chemistry Industry Merit Prize, University of British Columbia Department of Biochemistry

2006 – 2007 University of British Columbia Science Co-op Student of the Year Award (Finalist), University of British Columbia

2006 – 2007 Dr. Peter Gee-Pan Mar Memorial Scholarship, University of British Columbia Department of Biochemistry

2004 – 2007 Renewable National In-Course Award, Canadian Millennium Excellence Awards

2002 – 2003 & 2006 – 2007 Undergraduate Scholarship Program, University of British Columbia