

Melinda M. Diver, Ph.D.

Memorial Sloan Kettering Cancer Center
Assistant Member, Structural Biology

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 Mariani, 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, Orthopaedic 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 carboxymethyltransferase
- 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 carboxymethyltransferase
- 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 Undergraduate Scholarship Program, University of British Columbia
& 2006 – 2007