

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF CELL AND DEVELOPMENTAL BIOLOGY

Melanie D. Ohi, Ph.D., associate professor of cell and developmental biology, with tenure, Department of Cell and Developmental Biology, Medical School, is recommended for promotion to professor of cell and developmental biology, with tenure, Department of Cell and Developmental Biology, Medical School [also being promoted to research professor, Life Sciences Institute].

Academic Degrees:

Ph.D.	2002	Vanderbilt University
B.S.	1996	Pacific Lutheran University

Professional Record:

2017- present	Associate Professor of Cell and Developmental Biology, with tenure, University of Michigan
2017-present	Research Associate Professor, Life Sciences Institute, University of Michigan
2016-2017	Associate Professor of Biochemistry, without tenure, Vanderbilt University
2014-2017	Associate Professor of Cell and Developmental Biology, with tenure, Vanderbilt University
2007-2014	Assistant Professor of Cell and Developmental Biology, Vanderbilt University

Summary of Evaluation:

Teaching: Dr. Ohi is extensively involved in teaching. She presents lectures and moderates classroom discussions in the graduate level courses: Introduction to Structural Biology, BCHM300, Introduction to Modern Biological Microscopy, CBIO313, and the Graduate Seminar in Molecular Biophysics, BCHM349. For the last three years, she has been the course director for Special Topics in Cell Biology, Nobel Prize Winners, CBIO338. Dr. Ohi has also taught in the cross-disciplinary undergraduate course Nucleic Acid Transactions, BSCI265. For the past four years, she has served as a faculty mentor for Intensive Mentoring Program for Advancement and Career Training (IMPACT) where she meets weekly with ten students during their first year of graduate school to discuss, in a small group setting, successful transition strategies into graduate school, professionalism, and how to become a student scholar. For the last five years, Dr. Ohi has directed and organized the Structural Electron Microscopy Educational Group, which meets monthly and is open to all students, post-doctoral fellows, staff, and faculty interested in learning about cryo-EM.

In addition to Dr. Ohi's extensive experience in classroom instruction, she is very involved in teaching in her laboratory, providing hands-on training to postdoctoral fellows, graduate students, and undergraduate students. As the co-director of the University of Michigan's Cryo-EM facility and core, she has been instrumental in educating and training students, post-doctoral fellows, and research staff from across the university on how to apply these techniques to various experimental systems. Dr. Ohi has hosted 23 rotations students in her lab and has served or continues to serve on 33 graduate dissertation committees.

Research: Dr. Ohi's group is interested in understanding how large molecular machines are structurally organized and how this organization translates into function within the cell. Towards this

goal, her lab employs a wide range of approaches that include single particle cryo-electron microscopy, NMR analysis, biochemistry, X-ray crystallography, and yeast genetics. An ongoing focus of the lab has been to dissect the molecular organization and function of the spliceosome complexes involved in pre-mRNA splicing. The goal of her work is to generate a series of detailed snapshots of the spliceosome as it assembles, catalyzes the splicing reaction, and disassembles using a combination of biochemical, genetic, and structural strategies. This represents long-term research focus that has spanned her scientific career to date, starting in graduate school and continuing in her previous position as an associate professor at Vanderbilt University, and in her current position at the University of Michigan.

Yet another major focus of her research program has been to generate structure-based models of dynamic molecular machines found in infectious agents and required for pathogenesis. Structural snapshots of molecular machines required for bacterial pathogenesis are essential for the development of new therapeutic approaches that can block specific pathogenic processes. Dr. Ohi has become a national leader in this field, with publication of the structures of the *Helicobacter pylori* Cag Type IV Secretion System, the *Helicobacter pylori* VacA toxin, and the *Legionella pneumophila* Dot/ICM Type IV Secretion System. The research in her lab is currently supported by four multi-principal investigator R01 awards from the National Institutes of Health. Dr. Ohi routinely publishes in high-impact journals and is requested to write review articles as a thought-leader in the field of single particle cryo-EM.

Five Recent and Significant Publications:

Chung, J, Sheedlo, MJ, Campbell, AM, Sawhney, N, Frick-Cheng, AE, Lacy, DB, Cover, TL, Ohi, MD: Structure of the *Helicobacter pylori* Cag Type IV Secretion System. *eLife*. Jun 18;8. pii: e47644, 2019.

Su, M, Erwin, AL, Campbell, AM, Pyburn, TM, Saley, LE, Hanks, JM, Lacy DB, Akey, DL, Cover, TL, Ohi, MD: (2019) Cryo-EM analysis of *Helicobacter pylori* VacA shows structural basis of oligomerization. *Journal of Molecular Biology*. 431(10): 1956-1965, 2019.

Mittendorf, KF, Marinko, JT, Hampton, CM, Key, Z, Hadziselimovic, A, Schleich, JP, Law, CL, Li, J, Wright, ER, Sanders, CR, Ohi, MD: PMP22 Alters Membrane Architecture. *Science Advances*. 3(7): e1700220, 2017.

Pyburn, TM, Foegeding, NJ, Gonzalez-Rivera, C, McDonald, NA, Gould, KL, Cover, TL, Ohi, MD: Structural organization of membrane-inserted hexamers formed by *Helicobacter pylori* VacA toxin. *Molecular Microbiology*. 102(1):22-36, 2016.

Collier, SE, Voehler, M, Peng, D, Ohi, R, Gould, KL, Reiter, NJ, Ohi, MD: Structural and functional insights into the N-terminus of *Schizosaccharomyces pombe* Cdc5. *Biochemistry*. 53(41): 6439-51, 2014.

Service: Since joining the University of Michigan in 2017, Dr. Ohi has served as a leader of the Cryo-EM community here. She has participated on faculty search committees for the Department of Cell and Developmental Biology, and the Department of Molecular Physiology and Biophysics. Dr. Ohi is a member of the American Society of Cell Biology, the Biophysical Society, the Microscopy Society of America, and the American Society of Microbiology. She has also recently signed on to serve as the associate chair of the Department of Cell and Developmental Biology. Dr. Ohi is also highly sought after for service at the national level. She serves on the Awards

Committee and the 75th Anniversary Committee for the Microscopy Society of America. She was a guest editor for a special edition of *Methods* focused on the structure and function of the spliceosome. In addition, she performs peer-review of manuscripts for a large number of scientific journals. Dr. Ohi has served as an ad hoc reviewer for the NIH, National Science Foundation, Wellcome Trust, the United States-Israel Binational Science Foundation, and the Asthma United Kingdom Research Initiative. She served as an expert committee member on the 2017 Canada Foundation for Innovation's Fund Competition for Structural Biology. She has served on NIH P01 and P41 review panels and is currently a standing member of the NIH Macromolecular Structure and Function C study section.

External Reviewers:

Reviewer A: "Dr. Ohi is an excellent cryo-electron microscopist and structural biologist with the tenacity to focus on extremely challenging problems...Her recent structural papers on *Helicobacter* in eLife and JMB were superb, bringing new clarity to the mechanism of pore formation."

Reviewer B: "Dr. Ohi's work on the spliceosome at the time represented a quintessential example of an important but highly dynamic complex that has eluded most efforts at analysis. Dr. Ohi's was one of the few labs in the world that were able to make progress on understanding the structure and function of this complex. I have also followed Dr. Ohi's work on pore forming toxins quite closely as I have had to [sic] opportunity to work on several of these myself. I was particularly struck by the astonishing quality of the work she published on *C. Difficile* toxins...Dr. Ohi is an acknowledged world leader in the structure and function of type 4 secretion systems, and particularly in solving difficult structures using cryo-EM, as evidenced by a high rate of invited seminars and invitation to international meetings...Dr. Ohi is internationally recognized for her outstanding work on pore forming toxins, her excellent application of cryo-EM methods, is highly collaborative, makes very effective use of hybrid methods, and has a successful and well established research career."

Reviewer C: "[Dr. Ohi has a] long and well recognized track record in using single particle cryo-EM to address a number of very interesting and challenging biological questions. She has a very productive and rigorous research program in her laboratory that is well appreciated by the field...her scholastic accomplishments are among the best of her peer in any other academic institutions."

Reviewer D: "Melanie has brought a lively collaborative presence to Michigan, as illustrated by her recent paper on centromeric tri-nucleosomes and her 2018 paper on microtubule minus-end aster organization...Michigan very successfully brought Melanie from Vanderbilt, anchored a crucial realm of structural biology, and imported a superb program in molecular mechanisms of toxin action...Promotion to full professor...is very much in order."

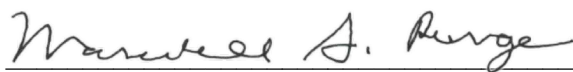
Reviewer E: "I have gained a high regard for Dr. Ohi's science, rigor and integrity. Her seminars are precise, clear and engaging. It is clear that Dr. Ohi is highly respected and is one of the leaders in the fields of cryoEM and macromolecular machines. She is unique in her range of expertise, which includes the technical side of cryoEM and a solid foundation in cell biology...I consider Dr. Ohi's work on the *H. phlori* protein complexes as outstanding and has made her a leader in the field of bacterial infection. Throughout Dr. Ohi's career, she has been highly successful in solving structures of complex molecular machines. This is due to her drive, intellect, expertise and clear vision of identifying crucial biological problems...generosity to share her expertise with colleagues, while maintaining a strong independent research program...well-regarded world-wide as an expert in cryoEM and applying this method to complex biological systems...her service record at the University of Michigan is stellar."

Reviewer F: “Dr. Ohi’s willingness to collaborate spreads the impact of her work in a variety of fields...I have also always been impressed by the very high standards Dr. Ohi holds for all of her work...Over her career, Dr. Ohio [sic] has made significant contributions to her discipline...She is a standing member of an NIH study section, which demonstrates her esteemed reputation and strong dedication to our nation’s biomedical research enterprise.”

Reviewer G: “Melanie has continued increasing the focus of her own research on membrane-associated complexes, particularly clinically relevant ones from *H. pylori*, the causative agent of peptic ulcers and the major risk factor for gastric cancer. She has made contributions to our understanding of both a pore-forming toxin secreted by *H. pylori*, and the bacterium’s secretion system. In a very nice paper published last year in eLife, her group solved the first structure of the *H. pylori* secretion system, revealing some unique features of this particular system but also providing insights into how substrates are secreted through these complex machines in general...cryo-EM remains challenging and the number of people with the know-how to use it well has not kept up with demand. This means that cryo-EM experts willing to collaborate can have a major impact on their community. Melanie is clearly one of these people, while at the same time maintaining her own vibrant research program...The depth and breadth of Melanie’s involvement are exactly what we look for in my own department when considering recruitments at the Professor rank.”

Summary of Recommendation:

Dr. Ohi has accomplished a record of truly exceptional scholarship. The high quality of her research and her expertise are broadly recognized by colleagues here as well as at other premier institutions, and have led to her recognition through the acquisition of several prestigious awards. She is an excellent teacher and mentor. I am pleased to recommend Melanie D. Ohi, Ph.D. for promotion to professor of cell and developmental biology, with tenure, Department of Cell and Developmental Biology, Medical School.



Marschall S. Runge, MD, PhD
Executive Vice President for Medical Affairs
Dean, Medical School

May 2021