

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF NEUROLOGY
DEPARTMENT OF MOLECULAR AND INTEGRATIVE PHYSIOLOGY

Michael M. Wang, M.D., Ph.D., associate professor of neurology, with tenure, Department of Neurology, and associate professor of molecular and integrative physiology, without tenure, Department of Molecular and Integrative Physiology, Medical School, is recommended for promotion to professor of neurology, with tenure, Department of Neurology, and professor of molecular and integrative physiology, without tenure, Department of Molecular and Integrative Physiology, Medical School.

Academic Degrees:

Ph.D.	1994	Johns Hopkins University
M.D.	1994	Johns Hopkins University
A.B.	1987	Harvard University

Professional Record:

2010-present	Associate Professor of Neurology and Associate Professor of Molecular and Integrative Physiology, University of Michigan
2003-2010	Assistant Professor of Neurology and Assistant Professor of Molecular and Integrative Physiology, University of Michigan
2002-2003	Assistant Professor of Neurology, Johns Hopkins University
2002-2003	Instructor of Anesthesiology/Critical Care Medicine, Johns Hopkins University
2000-2002	Instructor of Neurology, Johns Hopkins University

Summary of Evaluation:

Teaching: A major part of Dr. Wang's activities includes teaching at multiple levels and in diverse learning settings. He spends over 1000 hours per year devoted to teaching (mostly concurrent with research and clinical activity). In the research lab, he has mentored undergraduates, graduate students, medical students, post-doctoral fellows, and visiting scholars. Learners have achieved successful positions after leaving the lab (undergraduates have gained admission to graduate school and post-doctoral fellows have advanced to strong academic faculty positions). In clinical settings, Dr. Wang has also found success in teaching medical students, residents, and fellows while performing clinical work at the university and at the VA Ann Arbor Healthcare System. He teaches in a variety of clinical settings, including the outpatient clinic, the inpatient wards, and the Emergency Department for acute stroke codes. Dr. Wang's medical student and resident evaluations are outstanding and this is reflected in the scores and the comments he receives. Recent scores and comments from the medical student evaluations include 4.71 (mean 4.33) for "overall quality of teaching" and 4.76 (mean 4.37) for

“overall ability to serve as a role model.” In the classroom, Dr. Wang has taught undergraduates (UC256), graduate students (NS602), medical students (512REP, 512CAR, 512MUS, 508GAS, 510END, 512REN), and residents, lecturing in both formal courses and didactic sessions for clinical trainees in neurology, psychiatry, physical medicine and rehabilitation, and internal medicine. Of special note, he has taken on numerous teaching leadership roles. For example, as chief of neurology at the VA Ann Arbor, he is responsible for resident education for all UM neurology residents rotating at the VA; he was selected as Ph.D. thesis committee chair for a neuroscience graduate student; and he served as a course director for four years for NS602, a popular module of the required core curriculum taken by all Neuroscience Program graduate students.

Research: Dr. Wang’s research focuses on cerebrovascular disorders, an area of interest dating to his initial hire at the university in 2003. This research builds upon his dual training as a molecular and cellular biologist and as a neurologist. He is one of the few practicing vascular neurologists investigating the pathogenesis of human cerebral small vessel disease using biochemical and molecular approaches. Although the NIH estimates that cerebral small vessel disease affects a majority of elderly individuals, this is still a nascent area of investigation which lacks the resources available to more mature fields such as Alzheimer’s disease. Because of the limited history of small vessel research, Dr. Wang devoted extensive time to the development of reagents and tools required to initiate detailed studies of diseased human small vessels. Nevertheless, after overcoming these hurdles, Dr. Wang has made significant contributions to the field, describing multiple key molecular characteristics of CADASIL, an important genetic form of small vessel disease in humans. His lab has demonstrated the deposition of a half dozen new molecules (including collagen subtypes, von Willebrand factor, biglycan, and decorin) in blood vessels of CADASIL patients and has characterized the cellular effects these proteins in detail. The breadth and promise of this work has been recognized by federal funding agencies, which have supported the work via NIH K02, R21, and R01 grants and two VA Merit awards. Dr. Wang has been, according to NIH Reporter, the most highly funded investigator in the field of CADASIL research and is the only current awardee of a federal grant in this area. Building upon a CADASIL tissue bank that he started in 2009, together with novel antibodies that he has cloned, Dr. Wang plans to investigate conformational changes in the NOTCH3 protein in human small vessel disease. Further work in progress includes characterization of a series of newly identified proteins from human small blood vessels which may participate in disease pathology. Dr. Wang also conducts research on the physiological effects of stroke injury in animal models, in a long-standing collaboration with Dr. Jimo Borjigin in the Department of Physiology. Their work has elucidated new effects of stroke on circadian biology, sleep physiology, and brain connectivity; one of their collaborative studies is funded by another VA Merit awarded to Dr. Wang. A recent pair of their collaborative papers has garnered significant academic and media attention.

Recent and Significant Publications:

Borjigin J, Lee UC, Liu T, Pal D, Huff S, Klarr D, Sloboda J, Hernandez J, Wang MM, Mashour GA: Surge of neurophysiological coherence and connectivity in the dying brain. *Proceedings of the National Academy of Sciences* 110:14432-14437, 2013.

Meng H, Zhang X, Lee SJ, Wang MM: Von Willebrand Factor inhibits mature smooth muscle gene expression through impairment of Notch signaling. *PLoS One* 8:e75808, 2013.

Zhang X, Meng H, Wang MM: Collagen represses canonical Notch signaling and binds to Notch ectodomain. *International Journal of Biochemistry & Cell Biology* 45:1274-1280, 2013.

Zhang X, Lee SJ, Young KZ, Josephson DA, Geschwind MD, Wang MM: Latent NOTCH3 epitopes unmasked in CADASIL and regulated by protein redox state. *Brain Research* 1583:230-236, 2014.

Zhang X, Lee SJ, Young MF, Wang MM: The small leucine-rich proteoglycan BGN accumulates in CADASIL and binds to NOTCH3. *Translational Stroke Research* 6:148-55, 2015.

Service: In the area of organizational leadership, Dr. Wang is highly active in the VA Ann Arbor Healthcare System. At the VA, Dr. Wang serves as chief of the Neurology Service and is responsible for guiding the clinical, research, and teaching activities of the faculty. The VA Neurology Service has grown significantly under Dr. Wang and plays an important collaborative role in UM neurology activities. Dr. Wang also serves as the chair of the VA Ann Arbor Research and Development Committee, which is charged with oversight of all research activities at the institution. Other significant VA committee activities include: Clinical Executive Board, Chief of Staff Advisory Committee, Search Committee for ACOS/R, and Executive Quality Leadership Board. He served as the acting associate chief of staff for research during the summer of 2014. At the university, Dr. Wang is a member of multiple institution-wide committees: CVC Grant Review Committee, Student Biomedical Research Program Committee (as Neurology representative), Neuroscience Program Curriculum Committee, and the MSTP Career Advisory Panel. Within the Department of Neurology, he serves on the Appointments, Promotions and Awards Committee (APAC). Extramural service includes membership on two advisory boards for CADASIL advocacy, two journal editorial boards, and the NST-2 study section of NIH/NINDS (2008-2014). He has also served on multiple study sections for the VA and the American Heart Association.

Trained as a clinical neurologist with vascular neurology subspecialization, Dr. Wang cares for outpatients at UM and at the VA Ann Arbor and serves as inpatient attending physician at both institutions. He also provides on call services for the UM Comprehensive Stroke Center, a professional activity that includes emergent care for acute stroke patients. He treats CADASIL patients who are referred nationally to his CVC outpatient clinic. These clinical activities synergize well with his research and teaching activities, which aim to ultimately improve the future clinical care of neurological patients.

External Reviewers:

Reviewer A: "Dr. Wang has been one of the leading scientists in the field studying the mechanism underlying brain injury after stroke...His findings on the function of Notch signaling in small vessel diseases are his most novel and original studies and will impact the field for years to come."

Reviewer B: “Both is excellent record of publication and consistent funding record in this extremely competitive environment attest to his stature in the vascular biology community....I believe Dr. Wang’s work is careful and original. My visit to your institution confirmed that he is clearly held in high esteem by his peers locally, something mirrored nationally and internationally.”

Reviewer C: “He really is one of our leaders in translational cerebrovascular research. He is unique—teaching, seeing patients, and performing cutting-edge science. This promotion to full professor is well deserved.”

Reviewer D: “...Dr. Wang is a superb candidate for promotion. Looking forward, I sense that he has the perspectives and skills to become either an important participant in new national initiatives to understand the human brain and how it changes in disease or to take on more substantial academic leadership responsibilities.”

Reviewer E: “He has continued in a steady fashion to gather an exceptional number of scientific and professional accolades that among many others include NIH and American Heart Association awards and a VA merit award. He has remained funded over the years and continues to publish numerous high profile, refereed publications in prestigious scientific journals.”

Summary of Recommendation:

Dr. Wang has made substantial contributions to the University of Michigan’s missions of teaching, research, and service. As a teacher, he provides high quality instruction in the classroom, the clinics, and the lab, broadly across the learning spectrum. At the same time, he has taken on essential lead roles in core components of the education of Ph.D. students and residents. He has established a mature, productive research program that focuses on cerebral small vessel disease, and he has maintained continuous federal funding. Very importantly, he has provided essential leadership to the department and the institution in his role as chief of the Neurology Service at the VA Ann Arbor Healthcare System. I am pleased to recommend Michael M. Wang, M.D., Ph.D. for promotion to professor of neurology, with tenure, Department of Neurology, and professor of molecular and integrative physiology, without tenure, Department of Molecular and Integrative Physiology, Medical School.



Marschall S. Runge, M.D., Ph.D.
Executive Vice President
for Medical Affairs
Dean, Medical School

May 2016