Approved by the Regents
May 21, 2015

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF PEDIATRICS AND COMMUNICABLE DISEASES
DEPARTMENT OF HUMAN GENETICS

Donna M. Martin, M.D., Ph.D., associate professor of pediatrics and communicable diseases, with tenure, Department of Pediatrics and Communicable Diseases, and associate professor of human genetics, without tenure, Department of Human Genetics, Medical School, is recommended for promotion to professor of pediatrics and communicable diseases, with tenure, Department of Pediatrics and Communicable Diseases, and professor of human genetics, without tenure, Department of Human Genetics, Medical School.

Academic Degrees:

1996	M.D.	University of Michigan
1992	Ph.D.	University of Michigan

Professional Record:

2008-present	Associate Professor of Pediatrics and Communicable Diseases, University of Michigan
2008-present	Associate Professor of Human Genetics, University of Michigan
2003-2008	Assistant Professor of Pediatrics and Communicable Diseases, University of Michigan
2003-2008	Assistant Professor of Human Genetics, University of Michigan
2001-2003	Lecturer, Department of Pediatrics and Communicable Diseases, University of Michigan
2001-2003	Research Investigator, Department of Human Genetics, University of Michigan

Summary of Evaluation:

Teaching: Dr. Martin teaches in multiple venues in both the Department of Pediatrics and Communicable Diseases and the Department of Human Genetics. Dr. Martin has developed a truly outstanding record of education including medical student training in human genetics, didactic genetics lectures for pediatric residents and medical genetics residents, pediatrics grand rounds, and medical genetics grand rounds here at the University of Michigan. Students have given her outstanding evaluations for her well-prepared sessions. In her laboratory, she mentors undergraduates, Ph.D. candidate graduate students, post-doctoral fellows, and senior research associates, exploring developmental disorders of the nervous system. Dr. Martin is the director of the medical genetics residency program, a two-year program that provides clinical medical genetics training for physicians to achieve board certification through the American Board of Medical Genetics. This post, which she has held since November 2006, involves responsibilities for the education, recruitment and administrative oversight of medical genetics residents. Her commitment to education is outstanding. In relation to the Department of Human Genetics,

Dr. Martin has participated as a small group leader for the M1 medical student course on "Patients and Populations" (Tom Gelehrter, M.D., Course Organizer) since 2003, and was invited to give lectures for this series in the Fall of 2014. She has provided lectures on metabolic diseases and developmental brain disorders for HG 649 "Advanced Clinical Concepts in Medical Genetics." She also mentors genetic counseling students in the pediatric genetics clinic, and has assisted human genetics graduate students in seminar preparation as part of their coursework requirements.

Research: Dr. Martin's most distinguished accomplishments relate to research discoveries in the genetics of human developmental disorders. In 2005, her laboratory generated the first genetically engineered mouse models of the human congenital disorder CHARGE Syndrome, with the goals of exploring underlying molecular genetic mechanisms and potential treatments. They established that the mouse is an excellent model for CHARGE Syndrome and exhibits many of the same birth defects that affect vision, hearing, growth, and cardiac development. Further work characterizing these mice led to the important discovery that mice with mutations in the same gene (*Chd7*) that causes human CHARGE Syndrome exhibit inner ear abnormalities that resemble those observed in humans, and that they also have defects in the ability of inner ear neurons to reach their appropriate targets. It was discovered that by detailed analysis of specific developing tissues, CHARGE-like mice lose the ability to form specific subsets and types of neurons in the ear [3], nasal epithelium [4], and brain [5]. These insights have led to new and exciting hypotheses about how CHD7, which acts to remodel chromatin in the cell nucleus, may influence expression of other genes that regulate neural formation and development. Identification of these CHD7-regulated genes, and the underlying mechanisms involved in their expression, could lead to new therapies or interventions for the myriad sensory impairments (deafness, blindness) and behavioral disorders (autism, anxiety, obsessive-compulsive disorders) that affect individuals with CHARGE. Additionally, Dr. Martin's laboratory has generated induced pluripotent stem cells from patients with CHARGE and *CHD7* mutations, and plans to use them to explore basic mechanisms of chromatin biology. She has demonstrated that *CHD7* mutant fibroblasts can be effectively reprogrammed into pluripotent stem cells and that they retain the ability to different into neurons. This exciting new research will enable us to test hypotheses about CHD7 biology using human cells, and could led to improvements in therapies or diagnosis. This research has been generously funded by the National Organization for Hearing Research (NOHR), the Hearing Health Foundation (HHF), the National Institutes of Health (NIH), and the CHARGE Syndrome Foundation. Dr. Martin's scientific efforts have also led to productive and exciting collaborations with other researchers in the United States, Europe, Israel, and Japan, and opportunities for service on international grant reviews and advisory boards. Dr. Martin and her laboratory have shared mice and scientific reagents to promote and facilitate the study of CHD7 in CHARGE with over 15 other laboratories around the world.

Recent and Significant Publications:

Layman WS, McEwen DP, Beyer LA, Lalani SR, Fernbach SD, Oh E, Swaroop A, Hegg CC, Raphael Y, Martens JR, Martin DM: Defects in neural stem cell proliferation and olfaction in *Chd7* deficient mice indicate a mechanism for hyposmia in human CHARGE syndrome. *Human Molecular Genetics* 18:1909-1923, 2009.

Hurd EA, Poucher HK, Cheng K, Raphael Y, Martin DM: The ATP-dependent chromatin remodeling enzyme CHD7 regulates proneural gene expression and neurogenesis in the inner ear. *Development* 137:3139-3150, 2010.

Layman WS, Hurd EA, Martin DM: Reproductive dysfunction in a mouse model of CHARGE syndrome caused by decreased GnRH neurogenesis. *Human Molecular Genetics* 15:20:3138-3150, 2011.

Hurd EA, Micucci JA, Reamer EN, Martin DM: Delayed fusion and altered gene expression contribute to semicircular canal defects in *Chd7* deficient mice. *Mechanisms of Development* 129:308-323, 2012.

Micucci JA, Layman WS, Hurd EA, Sperry ED, Frank SF, Durham MA, Swiderski DL, Skidmore JM, Scacheri PC, Raphael Y, Martin DM: CHD7 and retinoic acid signaling cooperate to regulate neural stem cell and inner ear development in mouse models of CHARGE syndrome. *Human Molecular Genetics* 23:434-448, 2014.

Service: Dr. Martin provides extensive service in both the Department of Pediatrics and the Department of Human Genetics. At the national level, Dr. Martin is a permanent member of the NIH Developmental Brain Disorders Study Section. She has served as a reviewer for the Oak Ridge Laboratories, the National Science Foundation, the Israel Science Foundation and the Italian Telethon. She serves as chair of the Scientific Advisory Board for the CHARGE Syndrome Foundation, a national support organization, and for Deaf-Blind Central, the state-sponsored agency whose mission is to provide care and support for children with vision and hearing impairments and their families. Dr. Martin is currently the associate chair for the University of Michigan Biomedical Research Council. She has served on numerous committees for Human Genetics and Pediatrics, including admissions, awards, prelim exam, and executive committees. She is currently the associate director of the Medical Scientist Training Program. She is an active, contributing member in the Hearing, Balance, and Chemical Senses program, the Neuroscience program, the Center for Organogenesis, and the Cancer Center. She and her laboratory staff are regular contributors to Mouse Club, an interdisciplinary group that meets monthly to discuss scientific advances in mouse genetics, and Stem Cell Club.

External Reviewers:

Reviewer A: "... I highly recommend that Dr. Donna Martin be promoted to Professor with tenure. She is very deserving of this scientific standing, given her most recent accomplishments. Her contribution to medical genetics, genetic disease and the auditory and vestibular field has been critical in demonstrating the relevance of determining the mechanisms of disease."

Reviewer B: "I have high regard for Dr. Martin's capabilities, elegant work and appreciate her important contributions to this field...In addition to her creative research, Dr. Martin is an active physician and teaches. The list of her lectures is impressive and clearly she is devoting a significant part of her times to these important duties."

Reviewer C: "Dr. Martin is also a skilled medical geneticist. She runs the inpatient biochemical genetics service for an aggregate of about three months a year. This is a challenging role as newborns presenting with severe inborn errors of metabolism represent one of [the] true emergencies that medical geneticists encounter and requires the ability manage these very complex cases."

Reviewer D: "She has been productive, and pursued original research that has been published in highly regarded journals in the field. She has an outstanding record of service, including clinical service. It appears that she is poised to continue to make important and innovative scientific and translational contributions."

Reviewer E: "Her fantastic NIH funding in the current environment is an objective measure of what experts in the field think of her work. Dr. Martin's service to the institution is evident by her teaching activities to [a] diverse set of trainees ranging from medical students, MSTP students, residents, to undergraduate and graduate students...She is truly an outstanding physician-scientist and any institution would be lucky to have her."

Summary of Recommendation:

Dr. Martin is a leader in the field of medical genetics. She is lauded and respected by her colleagues locally, nationally and internationally. I strongly recommend Donna M. Martin, M.D., Ph.D. for promotion to professor of pediatrics and communicable diseases, with tenure, Department of Pediatrics and Communicable Diseases, and professor of human genetics, without tenure, Department of Human Genetics, Medical School.

James O. Woolliscroft, M.D.
Dean
Lyle C. Roll Professor of Medicine

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