Approved by the Regents
May 15, 2014

PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF HUMAN GENETICS
DEPARTMENT OF NEUROLOGY

Anthony Antonellis, Ph.D., assistant professor of human genetics, Department of Human Genetics, and assistant professor of neurology, Department of Neurology, Medical School, is recommended for promotion to associate professor of human genetics, with tenure, Department of Human Genetics, and associate professor of neurology, without tenure, Department of Neurology, Medical School.

Academic Degrees:

Ph.D.	2004	George Washington University and National Institutes of Health Joint Program in Genetics
B.S.	1992	University of Massachusetts

Professional Record:

2008-present	Assistant Professor of Human Genetics and Assistant Professor of Neurology, University of Michigan

Summary of Evaluation:

Teaching: Dr. Antonellis directly mentored ten trainees including two high school summer students, three undergraduate students, three Ph.D. students, one M.D./Ph.D. student, and one post-doctoral fellow. Each trainee has had their own independent research project and all former trainees have moved on to excellent positions. His service on thesis committees is strong, including 11 students total. Four are his own Ph.D. students and the other seven are for Ph.D. students in Human Genetics, Cell and Molecular Biology, and Neuroscience. Dr. Antonellis has taught six lectures per year for five years in HG542 (Molecular Basis of Human Genetic Disease) (25 students), given a lecture in HG 632 (Experimental Genetic Systems) for the past four years (over 12 students) and has mentored three to four students in the Student Seminar Series for the past five years. He also attended one Student Seminar a week throughout the academic year. As course director in Experimental Genetic Systems for the past four years, he arranged training program faculty to provide research talks to over 24 students, and developed all new lectures for the HG 542 course. He organized the weekly human genetics research presentations by trainees for two years. His teaching evaluations are outstanding and he received the Basic Science Teaching Award in Human Genetics last year.

Research: The overarching objective of Dr. Antonellis' research is to understand the mechanisms of normal peripheral nervous system development and diseases that cause peripheral neuropathy, including Charcot-Marie-Tooth (CMT) disease. CMT is a common peripheral neuropathy that affects motor and sensory function in the extremities (feet, lower legs, and hands). The major types of CMT are those that affect myelinating Schwann cells (CMT1) and those that affect peripheral nerve axons (CMT2). Dr. Antonellis' efforts are divided into two major areas: (1) Determining the role of tRNA charging enzymes in axonal peripheral neuropathy; and (2) Characterizing genes important for Schwann cell development and function. He has been productive in publications and externally funded in research. Since his initial appointment in 2008, Dr. Antonellis has published 19 papers, seven of which are first or last author. He has published in journals that are considered high impact in the fields of genetics and neuroscience: *Genome Research* (14.3), *American Journal of Human Genetics* (11.2), *PLoS Genetics* (8.5), *Human Molecular Genetics* (7.7), and *Journal of Neuroscience* (6.9). His record of external funding is strong. He has past funding from NIH, a NIH Pathway to Independence Award (K99/R00), and funding from several foundations. He is currently funded by the NIH as a PI on an R01, and is on track to obtain a second NIH R01 grant. Dr. Antonellis is a member of the American Society of Human Genetics, International Mammalian Genome Society, Peripheral Nerve Society and the Society for Neuroscience. His international reputation is emerging. He has had invitations to speak (UK, Australia); he serves on grant review panels (France, China), and conducts reviews for a broad range of journals. Internally, he is active in the community of investigators studying rare diseases.

Recent and Significant Publications:

Vester A, Velez-Ruiz G, McLaughlin HM, NISC Comparative Sequencing Program, Lupski JR, Talbot K, Vance JM, Züchner S, Roda RH, Fischbeck KH, Biesecker LG, Nicholson G, Beg AA, and Antonellis A: A loss-of-function variant in the human histidyl-tRNA synthetase (*HARS*) gene is neurotoxic in vivo. *Hum Mutat* 34:191–199, 2013.

Jones EA, Brewer MH, Srinivasan R, Krueger C, Sun G, Charney KN, Keles S, Antonellis A, and Svaren J: Distal enhancers upstream of the Charcot-Marie-Tooth type 1A disease gene *PMP22*. *Hum Mol Genet* 21:1581–1591, 2012.

McLaughlin, HM, Sakaguchi R, Giblin W, NIH Intramural Sequencing Center, Wilson TE, Biesecker L, Lupski JR, Talbot K, Vance JM, Züchner S, Lee YC, Kennerson M, Hou YM, Nicholson G, and Antonellis A: A recurrent loss-of-function alanyl-tRNA synthetase (*AARS*) mutation in patients with charcot-marie-tooth disease type 2N (CMT2N). *Hum Mutat* 33:244–253, 2012.

Hodonsky CJ, Kleinbrink EL, Charney KN, Prasad M, Bessling SL, Jones EA, Srinivasan R, Svaren R, McCallion AS, Antonellis A: SOX10 regulates expression of the SH3-domain kinase binding protein 1 (*Sh3kbp1*) locus in Schwann cells via an alternative promoter. *Molecular and Cellular Neurosciences* 49:85–96, 2011.

McLaughlin HM, Sakaguchi R, Liu C, Igarashi T, Pehlivan D, Chu K, Iyer R, Cruz P, Cherukuri PF, Hansen NF, Mullikin JC, NISC Comparative Sequencing Program, Biesecker LG, Wilson

TE, Ionasescu V, Nicholson G, Searby C, Talbot K, Vance JM, Züchner S, Szigeti K, Lupski JR, Hou YM, Green ED, Antonellis A: Compound heterozygosity for loss-of-function lysyl-tRNA synthetase mutations in a patient with peripheral neuropathy. *Am J Hum Genet* 87:560–566, 2010.

Service: In the Department of Human Genetics, Dr. Antonellis has served on the Program in Biomedical Sciences (PIBS) Admissions Committee for five years (2008-2013) and the Human Genetics Faculty Recruitment Committee for four years (2008-2012). He serves on the career development committees for two MICHR Post-doctoral Translational Scholars Program awardees. In addition, he has served on seven preliminary exam committees (four as chair) for Human Genetics, Cell and Molecular Biology, and Neuroscience, and served one year on the Human Genetics Preliminary Exam abstract review committee. For the last two years, Dr. Antonellis organized the Human Genetics Friday Afternoon Seminar Series (FASS) and the annual Department of Human Genetics Retreat. Dr. Antonellis has given numerous talks, including those at the University of Miami Miller School of Medicine, Case Western University, the National Institutes of Health, and workshops on Charcot-Marie-Tooth disease and amyotrophic lateral sclerosis. His laboratory has had a total of five abstracts selected for talks at national and international meetings, and he was invited to write a review on tRNA synthetase mutations in human disease for *Current Opinion in Genetics and Development*. For the last two years, he has reviewed abstracts for the annual meeting of the American Society of Human Genetics and co-chaired two sessions at this meeting as well as at the Peripheral Nerve Society meeting. He has served as a reviewer for grant applications for the Association Française contre les Myopathies (Paris) and the Research Grants Council (Hong Kong), and as an outside thesis examination reader for three students at the University of Sydney, Australia. Dr. Antonellis served as an *ad hoc* manuscript reviewer for 23 journals including the *New England Journal of Medicine*, the *American Journal of Human Genetics* and *Genome Research*.

External Reviewers:

Reviewer A: "...his work to date has had a major impact on the field, resulting in seminal advances particularly with regards to establishing the role that mutations of tRNA synthetases play in the pathogenesis of peripheral neuropathies."

Reviewer B: "...I believe that Dr. Antonellis is a highly regarded international leader in our field and he is exactly the type of researcher that the University of Michigan should be proud to include among its tenured senior research faculty....His efforts and those of his laboratory have had a major impact on the field of neurology; most specifically he has made seminal contributions to our understanding of the role of *ARS* mutations and *Sox10* in peripheral nerve disease."

Reviewer C: "In terms of his rank among other scholarly professionals, he clearly is a world authority in this specific area of tRNA abnormality and inherited neurodegenerative conditions and has really no equivalent peers on this subject....He has presented and continues to present at many national and international meetings and has been provided a number of awards...It is often a great sign when such an accomplished scientist actually is involved in teaching, and this makes him exceptional in his field."

Reviewer D: "Dr. Antonellis has been the foremost investigator that has shown that mutations in a number of inherited neuropathies are caused by tRNA synthetase mutations....Dr. Antonellis is noted for his excellent mentoring and has or is currently mentoring a number of [junior] talented scientists that frequently present at national and international meetings."

Reviewer E: "He has supervised and being [sic] a member of PhD committees of more than 20 students, which is a quite impressive number of PhDs. Importantly, Dr. Antonellis was also an outside reader of three PhD thesis examinations in Sydney, Australia, demonstrating his international recognition as an external jury member."

Reviewer F: "He has been productive, and pursued original research that has [been] published in top journals in the field. There is no doubt that he will continue to make important, significant and innovative scientific contributions."

Summary of Recommendation:

Dr. Antonellis is developing an international reputation for his research and is an excellent citizen in teaching and service. He has been consistently funded and productive since joining the University of Michigan. We expect his trajectory to continue upward, and to be attractive for future funding based on the strong relevance of his research to this common, and devastating human disease. I am pleased to recommend the promotion of Anthony Antonellis, Ph.D. to associate professor of human genetics, with tenure, Department of Human Genetics, and associate professor of neurology, without tenure, Department of Neurology, Medical School.

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

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