Approved by the Regents
May 17, 2018

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

Anthony Antonellis, Ph.D., associate professor of human genetics, with tenure, Department of Human Genetics, and associate professor of neurology, without tenure, Department of Neurology, Medical School, is recommended for promotion to professor of human genetics, with tenure, Department of Human Genetics, and 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
B.S.	1992	University of Massachusetts

Professional Record:

2014-present	Associate Professor of Human Genetics, University of Michigan
2014-present	Associate Professor of Neurology, University of Michigan
2008-2014	Assistant Professor Human Genetics, University of Michigan
2008-2014	Assistant Professor of Neurology, University of Michigan

Summary of Evaluation:

Teaching: Dr. Antonellis' impact on scientific education in the Medical School has been substantial. He has been a course director and primary lecturer for eight years in the Department of Human Genetics core course, HG542 ("Molecular Basis of Human Genetic Disease"). He has been a course director and lecturer in HG632 ("Experimental Genetic Systems") for five years, and has been a lecturer in HG803 ("Advanced Topics in Genetics") for four years. Additionally, he has been a primary mentor for ~four students per year in the departmental seminar training courses HG821/HG822 ("Student Seminar Series"). Dr. Antonellis was the primary organizer and mentor for the student research seminar series (Friday Afternoon Seminar Series). In his didactic teaching interactions, Dr. Antonellis is noted for his extensive preparation and engaging participation; consequently, he has received strongly positive student evaluations. He was recognized for these educational efforts by earning the Basic Sciences Teaching Award in Human Genetics. Dr. Antonellis is the co-director of the NIH-supported Genetics Training Program. During his tenure in this position, the program – that has been continuously funded for over 43 years – was again renewed by NIH. He has co-organized the annual Genetics Training Program courses HG630 ("Genetics Short Course") and HG631 ("Genetics Program Student Seminar Series"). Outside of the Department of Human Genetics, he has co-directed and been a student mentor in CMB850, for the Cellular and Molecular Biology program. Dr. Antonellis has mentored multiple doctoral, master's, and undergraduate trainees in his laboratory. Since his promotion to associate professor in 2014, he has mentored four undergraduates, two master's program students, three PIBS rotation students, and has been the primary doctoral thesis mentor for four students. He has served on nine Ph.D. doctoral thesis committees since 2014, and 12 overall. In 2017, he accepted the leadership role as the associate chair for education. In this position, he oversees and

co-ordinates all educational activities in the department. The department has active Ph.D., M.S., and M.S.-Genetic Counseling training components. He has been instrumental in linking these distinct programs with a core curriculum, plus, separate, tailored training activities. Dr. Antonellis is strongly committed to advancing the depth and breadth of education in the field of human genetics. Additionally, Dr. Antonellis has a commitment to international education. He has been a Ph.D. thesis defense opponent for the University of Finland Faculty of Medicine, and an external thesis examination reader for the University of Sydney and Macquarie University (Australia).

Research: Dr. Antonellis' research work is widely recognized as highly imaginative and original. He has made fundamental contributions to the understanding of inherited human peripheral neuropathies and to the identification of their genetic causes. His broad knowledge and skills have impacted work across multiple disciplines, producing novel strategies and methods for examining human neurological disease. The overarching objective of Dr. Antonellis' research is to understand the mechanisms of the development of the peripheral nervous system and to determine the causes of peripheral neuropathy disease, including Charcot-Marie-Tooth (CMT). 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 study both types, specifically his efforts target: (1) determining the role of tRNA-charging enzymes in axonal peripheral neuropathy; and (2) characterizing the genes important for Schwann cell development and function. As of October 2017, he has 57 publications, including 51 peer-reviewed manuscripts, four review articles, and one book chapter. His laboratory has produced 13 peer-reviewed manuscripts, including four with Dr. Antonellis as a senior author, since his appointment as associate professor. Dr. Antonellis has built a strong and efficient research team in his laboratory, with a consistent production of senior-leadership research and collaborative work. Dr. Antonellis is noted for his novel research strategies and his facility for interdisciplinary collaboration. He is one of a small cadre of scientists at the university that uses the zebrafish as a genetic and developmental system. He is a member of collaborative groups that examine the spectrum of mutation in the human population using exome sequencing. He is also a member of the Charcot-Marie-Tooth International Consortium. Dr. Antonellis has uncovered the genetic and molecular basis for CMT disease in approximately 10 affected families. His work involves University of Michigan faculty in Neurology (Dr. B. Callaghan and Dr. S. Ramchandren) seeking to identify additional families with peripheral neuropathy using advanced technology genetic studies. Dr. Antonellis has an unbroken and continuing record of funding from NIH. Since 2013, Dr. Antonellis has served as the principal investigator on two R01 and one R21 grants, and co-investigator on one R01. He has been strongly funded by non-governmental foundations, including grants from the Muscular Dystrophy Association, the Dystonia Medical Research Foundation, and the United States-Israel Binational Science Foundation.

Recent and Significant Publications:

Brewer MH, Ma KH, Beecham GW, Gopinath C, the Inherited Neuropathy Consortium (INC), Baas F, Choi BO, Reilly MM, Shy ME, Züchner S, Svaren J, Antonellis A: Haplotype-specific modulation of a SOX10/CREB response element at the Charcot-Marie-Tooth disease type 4C locus SH3TC2. *Hum Mol Genet* 23:5171-5187, 2014.

Griffin LB, Sakaguchi R, McGuigan D, Gonzalez MA, Searby C, Züchner S, Hou YM, Antonellis A: Impaired function is a common feature of neuropathy-associated glycyl-tRNA synthetase mutations. *Hum Mutat* 35:1363-1371, 2014.

Simons C*, Griffin LB*, Helman G, Golas G, Pizzino A, Bloom M, Murphy JLP, Crawford J, Evans SH, Topper S, Whitehead MT, Schreiber JM, Chapman KA, Tifft C, Lu KB, Gamper H, Shigematsu M, Taft RJ, Antonellis A, Hou YM, Vanderver A: Loss-of-function alanyl-tRNA synthetase mutations cause an autosomal recessive early onset epileptic encephalopathy with persistent myelination defect. *Am J Hum Genet* 96:675-681, 2015.

Fogarty EA*, Brewer MH*, Rodriguez-Molina JF, Law WD, Ma KH, Steinberg NM, Svaren J, Antonellis A: SOX10 Regulates an alternative promoter at the Charcot-Marie-Tooth disease locus MTMR2. *Hum Mol Genet* 25:3925-3936, 2016.

Oprescu SN, Chepa-Lotrea X, Takase R, Golas G, Markello TC, Adams DR, Toro C, Gropman AL, Hou YM, Malicdan MCV, Gahl WA, Tifft CJ, Antonellis A: Compound heterozygosity for loss-of-function GARS variants results in a multi-system developmental syndrome that includes severe growth retardation. *Hum Mutat* 38:1412-1420, 2017.

Service: Dr. Antonellis is an exemplary citizen in the Department of Human Genetics, the Medical School, and the international scientific community. He is currently the associate chair for Education in the Department. Dr. Antonellis co-chairs the four standing committees on education (one for each program and one for curriculum). Dr. Antonellis has been a member of the Chair's Advisory Committee since 2014. At the Medical School, he continues to serve as a program committee member for the interdisciplinary Cellular and Molecular Biology program and as the co-director of the Genetics Training Program. Dr. Antonellis has had significant impact in the community of human geneticists. The major national (and international) organization in the field is the American Society of Human Genetics (ASHG). Within ASHG, Dr. Antonellis has served continuously since 2012, as a meeting session chair, a poster session reviewer, a Program Committee member, and last year as the annual meeting program committee chair, overseeing the scientific content for a meeting with over 7000 attendees. Dr. Antonellis is a widely-used reviewer of manuscripts and research grant proposals including work with the journals *Human Molecular Genetics*, *American Journal of Human Genetics*, *PLOS One*, *Genome Research*, *Neuroscience*, and the *Journal of the American Medical Association*. Grant review panels include ad hoc membership with Association Française Contre les Myopathies (France), Medical Research Council (UK), and the Center for RNA Biomedicine (Univ. Michigan), and, with the National Institutes of Health, review panels on "Neurodevelopment, Synaptic Plasticity, and Neurodegeneration – ZRG1-F03A", "Innovative Therapies and Tools for Screenable Disorders – ZRG1 GGG-K", and "Therapeutic Approaches to Genetic Diseases."

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 rRNA synthetases play in the pathogenesis of peripheral neuropathies."

Reviewer B: "…Tony is increasingly sought after as a seminar speaker or as an invited speaker at national/international meetings, and his involvement as a leader in different organizations…speaks to his presence in the scientific community."

Reviewer C: "Dr. Antonellis has published numerous papers from his lab, with several focusing on the roles of aminoacyl-tRNA synthetase variants in human disease. Dr. Antonellis has built a strong track record in this field and is now widely respected as one of the leaders in the area."

Reviewer D: "Dr. Antonellis is currently one of the most authoritative scientists in the human genetics of aminoacyl-tRNA synthetases. More importantly, unlike many human geneticists, Dr. Antonellis goes many steps further after the initial discovery of genetic mutations. He has developed different *in vitro* and *in vivo* models to further investigate the underlying cell biology and molecular mechanisms of these diseases in the peripheral nerves, which is particularly impressive to me. It also demonstrates his willingness and creativity in crossing different scientific areas."

Reviewer E: "His approach is comprehensive, and his publications contain beautiful data. Consequently, several of his publications have had a high degree of impact in the field….He has been productive, and pursued original research that has [been] published in top journals in the field. He is recognized as an excellent investigator in human genetics. There is no doubt that he will continue to make important, significant and innovative scientific contributions."

Summary of Recommendation:

Dr. Antonellis is a well-funded, internationally-recognized, and productive scientist. He has sustained a record of high impact work in the field of peripheral neuropathy, at the level of both neurons and Schwann cells. He has served the scientific community as a leader in organizing and sustaining the largest annual meeting in the field of human genetics. I am pleased to recommend Anthony Antonellis, Ph.D. for promotion to professor of human genetics, with tenure, Department of Human Genetics, and professor of neurology, without tenure, Department of Neurology, Medical School.

Marschall S. Runge

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

May 2018