

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF NEUROLOGY

Peter K. Todd, M.D., Ph.D., assistant professor of neurology, Department of Neurology, Medical School, is recommended for promotion to associate professor of neurology, with tenure, Department of Neurology, Medical School.

Academic Degrees:

M.D./Ph.D.	2004	University of Wisconsin, Madison
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Professional Record:

2010-present	Assistant Professor of Neurology, University of Michigan
2008-2009	Clinical Lecturer, Department of Neurology, University of Michigan

Summary of Evaluation:

Teaching: Dr. Todd directed the year-long neuroscience science course for the neurology residents from 2010-2014. He now directs the Neuropathology section of NS602 Principals of Neuroscience course for neuroscience graduate students. Dr. Todd gives one to three, one hour lectures each year to neurology residents as part of the Basic Neuroscience conference series. He is a lecturer in the first year biochemistry course for Medical Scientist Training Program Students, Biochem 552. He gives lectures annually in two separate upper-level undergraduate courses. In Neuro 455 (Neurobiology of Parkinson Disease) he gives one two hour lecture and leads one two hour discussion. In MCDB 455 (Cell biology of neurodegeneration), he gives one two hour lecture. He also gives a one hour lecture to the genetic counseling students on the genetics of dementia.

On the national stage, Dr. Todd has served as a lecturer and mentor at the AUPN/AAN Research Career Development Symposium held before the American Academy of Neurology meeting for the past five years. He has directed or taught in courses at the 2010, 2012, and 2014 American Academy of Neurology Annual Meetings, the 2015 American Neurological Association Annual Meeting, and the 2011 and 2012 Movement Disorders Society Annual Meeting. Dr. Todd is chairing a special "Future of Neurology" program on Precision Neurology at the AAN meeting this spring.

Over the past six years, Dr. Todd has served as the primary research mentor for 13 undergraduate students and ten graduate students, four of whom have chosen to join his laboratory for their thesis. In sum, Dr. Todd is an able teacher who is well prepared and eager to educate and counsel students and residents across a wide number of disciplines in medicine and research. Both medical students and residents find their time with Dr. Todd beneficial to their education. Everyone recognizes his depth and breadth of knowledge, and with experience the numerical grading of his teaching has improved, consistently greater than 4 on a 5 point scale in recent years.

Research: Dr. Todd's laboratory studies inherited neurological disorders with a central goal of developing novel therapeutics for these conditions. His work focuses primarily on the roles of RNA biology in neuronal function and nervous system disease through studies on non-exonic nucleotide repeat expansion disorders. In these disorders, the repeats are expressed as RNA but are not located within the annotated coding region of associated genes. These repeats elicit neurodegeneration through three mechanisms. First, as DNA the repeats can influence the transcription of the genes in which they reside and thus alter local gene expression. Second, the repeats as RNA can sequester RNA binding proteins and prevent them from performing their normal functions. Third, despite existing in putatively "noncoding" regions of transcripts, they can support translational initiation in the absence of an AUG initiation codon through a process known as "RAN translation" that our group was involved in discovering. The Todd lab utilizes biochemical, cellular and molecular genetics techniques combined with *Drosophila*, mouse and human ES and iPS based model systems to determine the relative contributions of each of these pathogenic mechanisms to disease biology and to understand their broader relevance to neurobiology and neurologic disease.

Current funded research focuses on three disorders: Myotonic Dystrophy type 1 (DM1), Fragile X-associated Tremor/Ataxia Syndrome (FXTAS) and C9orf72-associated Amyotrophic Lateral Sclerosis and Frontotemporal Dementia (C9 FTD/ALS). For FXTAS and C9 FTD/ALS, we have active projects addressing three specific questions: 1) What are the contributions of RAN translation to disease pathogenesis and how is it mediated mechanistically? 2) How do repeat expansions alter the normal regulation, translation, and function of the genes in which they reside? 3) What is the relationship between RNA repeat elicited toxicity and RAN translation elicited toxicity?

Over the past six years, the Todd lab has published 20 peer reviewed research papers and there are currently 13 people in it, including four graduate students, three post-doctoral fellows, one technician and five undergraduates. They are highly collaborative with investigators at Michigan and around the world. Dr. Todd has been successful at obtaining significant independent research funding since joining the faculty. He received a K08 award in 2010 that finished this year. He received an R01 that started in April 2014. He has obtained two VA merit awards: one on Fragile X-associated Tremor Ataxia syndrome another on C9orf72-associated ALS. He received private foundation grants from the Muscular Dystrophy Association, Pilot Grants from the Michigan Alzheimers Disease Center and the Michigan Protein Folding Disease Initiative, and philanthropic funding from a private donor. Dr. Todd also serves as a mentor on numerous NIH and private foundation pre-doctoral and post-doctoral fellowships and training grants.

Recent and Significant Publications:

Todd PK, Oh S-Y, Krans A, Pandey UB, DiProspero NA, Min K-T, Taylor JP, Paulson HL: Histone deacetylases suppress CGG repeat-induced neurodegeneration via transcriptional silencing in models of Fragile X tremor ataxia syndrome. *PLoS Genetics* 6:e1001240, 2010.

Todd PK, Oh S-Y, Krans A, He F, Sellier C, Frazer MI, Renoux AJ, Chen K-C, Scaglione KM, Basrur V, Elenitoba-Johnson K, Vonsattel JP, Louis ED, Sutton MA, Taylor JP, Mills RE, Charlet-Berguerand N, and Paulson HL: CGG repeat associated translation mediates neurodegeneration in fragile X tremor ataxia syndrome. *Neuron* 78:440-455, 2013.

Illiff AJ, Renoux AJ, Krans A, Usdin K, Sutton MA, Todd PK: Impaired activity-dependent FMRP translation and enhanced mGluR-dependent LTD in Fragile X premutation mice. *Human Molecular Genetics* 22:1180-1192, 2013.

He F, Krans A, Freibaum BD, Taylor JP, Todd PK: TDP-43 suppresses CGG repeat-induced neurotoxicity through interactions with HnRNP A2/B1. *Human Molecular Genetics* 23:5036-5051, 2014.

Oh S-Y, He F, Krans A, Frazer M, Taylor JP, Paulson HL and Todd PK: RAN translation at CGG repeats induces ubiquitin proteasome system impairment in models of fragile X-associated tremor ataxia syndrome. *Human Molecular Genetics* 24:4317-4326, 2015.

Service: Within the Department of Neurology, Dr. Todd directs the Neurogenetics Clinical Research Program, which is aimed at augmenting research on genetic causes of neurological disease within the university as well as addressing the emerging roles of new sequencing technologies in neurological practice both within the university and nationally. In addition to his course directorships, he served on the admissions committee for the Neuroscience Graduate Program (2013-2015), on seven graduate student thesis committees, and on three graduate student preliminary exam committees. He participates regularly on campus in a number of seminar series and presents in some of these forums, including Neurology Grand Rounds, the Neurodegenerative Disease Research Series, the RNA supergroup, and the Fragile X and Neurodevelopmental interest group. Outside the university, Dr. Todd has given Grand Rounds or equivalent talks at multiple universities around the world. He has been an invited speaker at the AAN, the ANA, the MDS, the Japanese Neurological Society, the Japanese society of neurochemistry, the CAG Gordon conference, and the CSHL meeting on Translational Control. He regularly serves as an ad hoc member of the NIH CMND Study Section and reviews grants for numerous disease foundations. He is a member of the translational neuroscience committee at the American Academy of Neurology (AAN), is co-chair of the Movement Disorders Special interest group at the American Neurological Association (ANA), and serves on the national FXTAS Task Force.

Dr. Todd is a Staff Physician at the VA Medical Center in Ann Arbor where he works in a busy neurodegenerative disease clinic focused on Parkinson's Disease and related movement disorders as well as Alzheimers disease and related dementias. He sees patients in this clinic one half day per week. Additionally, Dr. Todd co-founded and serves as co-director of the Fragile X Clinic at the University of Michigan, in which he sees adult patients with Fragile X Syndrome and FXTAS. This clinic is now part of a National Fragile X Clinical Research Consortium funded by the CDC and is participating in the first ever clinical trial on a drug for Fragile X Syndrome at the university. Dr. Todd regularly fields emails and phone calls from across the country from patients with FXTAS who have questions about their diagnosis and management. He also co-directs the Ataxia Clinic at the University of Michigan and sees patients in this clinic two half days per month. In addition to these outpatient clinical duties, Dr. Todd takes call at the VA for seven weeks of the year. He also serves as attending on either the inpatient Neurology ward or the neurology consult service for two to four weeks each year.

External Reviewers:

Reviewer A: "Dr. Todd's scholarship is solid, and he has clearly been very active as a researcher in the area of RNA and RAN-peptide toxicity, especially in Fragile X syndrome....he has clearly been successful in obtaining outside funding for his work, and contributes significantly to the academic community at the University of Michigan, and nationwide."

Reviewer B: “Dr. Todd is known by others as an international authority on molecular mechanisms in fragile X tremor ataxia syndrome (FXTAS) and fragile X syndrome, two rare degenerative and developmental diseases...Dr. Todd has delivered more than 30 national and international invited conferences and professorships in Europe, US, in South America on these topics.”

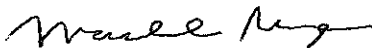
Reviewer C: “His 2013 publication entitled ‘*CGG repeat-associated translation mediates neurodegeneration in fragile X tremor ataxia syndrome*’ is a milestone achievement. It provided a completely new mechanistic insight that altered the way the field views the origins of pathogenesis.”

Reviewer D: “I believe Peter to be one of the top [of his cohort] investigators working on neurological/neurodegenerative disease. That he is a physician scientist adds further to his strength and value to any major research institution....There is clear evidence of the quality and significance of his scholarly activity, and he has a national and international reputation that continues to increase in stature. Peter would be a top candidate for promotion at any major research institution.”

Reviewer E: “...Dr. Todd has successfully evolved as a physician excelling in care, teaching and research. He has established himself as an educator and scientist at the national level. His publication record and grant funding are outstanding.”

Summary of Recommendation:

Dr. Todd has become an internationally recognized expert in the field of nucleotide repeat expansion disorders. He is particularly recognized for his work on Fragile X-associated Tremor Ataxia Syndrome (FXTAS). His discovery of how the CGG repeat which causes FXTAS leads to the hallmark pathology in this disorder has significantly reshaped the focus of research on this disorder and has laid the groundwork for new pathways of therapy development. He plays an active role in the leadership of the American Academy of Neurology and the American Neurological Association, including important mentorship roles for aspiring physician scientists in the neurosciences. I am pleased to recommend Peter K. Todd, M.D., Ph.D. for promotion to associate professor of neurology, with tenure, Department of Neurology, Medical School.



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

May 2016