Approved by the Regents
May 21, 2020

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

Catherine E.H. Keegan, M.D., Ph.D., associate professor of pediatrics, with tenure, Department of Pediatrics, and associate professor of human genetics, without tenure, Department of Human Genetics, Medical School, is recommended for promotion as professor of pediatrics, with tenure, Department of Pediatrics, and professor of human genetics, without tenure, Department of Human Genetics, Medical School.

Academic Degrees:

M.D.	1996	University of Michigan
Ph.D.	1996	University of Michigan
B.S.	1988	University of Michigan

Professional Record:

2011-present	Associate Professor of Pediatrics, University of Michigan
2011-present	Associate Professor of Human Genetics, University of Michigan
2009-2011	Assistant Professor of Human Genetics, University of Michigan
2004-2011	Assistant Professor of Pediatrics, University of Michigan
2004-2004	Clinical Lecturer of Pediatrics, University of Michigan
2002-2004	Lecturer of Pediatrics, University of Michigan

Summary of Evaluation:
Teaching: Dr. Keegan's commitment to education is exceptionally broad, which attests to her outstanding capabilities with learners at different stages of development. Her teaching activities consist of classroom instruction, research instruction in the laboratory, and clinical instruction of medical students, residents and fellows. Her clinical instruction includes supervision of third year and fourth year medical students rotating through the Outpatient Pediatric Genetics Clinic, and while attending on the Inpatient Pediatrics Genetics service. Dr. Keegan has supervised pediatric residents caring for patients with inborn errors of metabolism on the genetics inpatient service, supervised and taught medical genetics fellows, and regularly participates in the clinical genetics grand rounds. Her classroom instruction includes teaching several masters and graduate student level Human Genetics courses, including Human Genetics 640- GC Sem I: Clin Skills, Human Genetics 651- Medical Genetics II, and Human Genetics 803- Adv Topics Genetics. She leads pediatric resident Morning Report Conference Genetics cases, the third year medical student core Pediatrics Curriculum Genetics lecture, and the first year medical student Reproduction/ Embryology sequence, Urogenital Development.

In the laboratory, Dr. Keegan has supervised undergraduate and graduate students, post-doctoral and clinical fellows. Since promotion to associate professor, she has served on seven dissertation committees. Dr. Keegan has also held several important and significant educational

administrative positions, including medical director of the Genetic Counseling Program from 2011-2016, and educational lead for the Division of Pediatric Genetics from 2006-2015. Since 2012, she has served as the associate director of the Medical Scientist Training Program, and as the program director of the Medical Genetics Residency Program since 2017.

Research: Dr. Keegan's research interests are focused on understanding the mechanisms that lead to birth defects in humans, and she is an international renowned leader in the fields of telomere biology and caudal development in humans and mice. Most recently, Dr. Keegan and her laboratory have made important and impressive contributions that have led to better understanding of caudal malformations. She has shown that the retrotransposon disruption of an enhancer in the Danforth mouse is associated with dysregulated Hedgehog signaling in early tail bud development. This is an important new mechanistic insight that will continue to contribute to the field's understanding of this developmental dysregulation. Dr. Keegan has a strong record of extramural research funding through the NIH, foundation and industry grants and institutionally. She has published more than 57 peer-reviewed articles in high profile genetics journals including *Human Molecular Genetics*, the *American Journal of Medical Genetics*, and *Gene*. In recognition of her expertise in her field, Dr. Keegan has been invited to present her research on 20 occasions regionally and nationally. She was honored with the Benz Birth Defects Research Award in 2018, and the Charles Woodson Collaborative Research Award in 2019 from the Department of Pediatrics.

Recent and Significant Publications:

Orchard P, White JS, Thomas P, Mychalowych A, Kiseleva A, Hensley J, Allen B, Parker SCJ*, Keegan CE*: Genome-wide chromatin accessibility and transcriptome profiling show minimal epigenome changes lead to coordinated transcriptional dysregulation of hedgehog signaling in Danforth's short tail mice, *Human Molecular Genetics* 28(5): 736-750, 2019. *Co-corresponding authors.

Granados A, Alaniz VI, Mohnach L, Barseghyan H, Vilain E, Ostrer H, Quint EH, Chen M, and Keegan CE: *MAP3K1*-related gonadal dysgenesis: Six new cases and review of the literature, *Am J Med Genet C Semin Med Genet*. Jun; 175(2):268-278, 2017.

**Kocak H, **Ballew BJ, **Bisht K, Eggebeen R, Hicks BD, Suman S, O'Neil A, Giri N, NCI DCEG Cancer Genomics Research Laboratory, NIC DCEG Cancer Sequencing Working Group, Maillard I, Alter BP, Keegan CE, *Nandakumar J, *Savage SA: Hoyeraal-Hreidarsson syndrome caused by germline mutation in the TEL patch of the telomere protein TPP1, *Genes Dev.,* 28(19) 2090-2102, 2014. **Co-first authors, *Co-corresponding authors.

Jones M, Osawa G, Regal JA, Weinberg DN, Taggart J, Kocak H, Friedman A, Ferguson DO, *Keegan CE, *Maillard I: Hematopoietic stem cells are acutely sensitive to *Acd* shelterin gene inactivation, *J. Clin. Invest.* 124(1): 353-366, 2014. *Co-corresponding authors

Vlangos CN, Siuniak A, Robinson D, Chinnaiyan A, Lyons RL, Cavalcoli J, Keegan CE: Next Generation Sequencing Identifies the Danforth's Short Tail Mouse Mutation as a Retrotransposon Insertion Affecting Ptf1a Expression. *PLoS Genetics* 9(2), 2013.

Service: Dr. Keegan is an exceptional physician whose clinical work focuses on the care of patients with a wide variety of known or suspected genetic disorders. Her clinical commitments are broad, encompassing general genetics, inborn errors of metabolism, Outreach Genetics activities, inpatient care and inpatient on call consult duties, and she has significant expertise in genetic evaluation of patients with Disorders of Sex Development and caudal malformations. Complementary to her clinical and research focus, Dr. Keegan served as the director of the Disorders of Sexual Development Clinical Program from 2013-2018. She has established a significant track record of international, national and institutional service. She has participated in multiple study sections for the NIH, has served on several NIH special emphasis panels, served as an ad hoc grant reviewer for the American Cancer Society, and for Great Ormond Street Hospital Children's Charity, internationally. She has also reviewed abstracts and has chaired scientific sessions for the American Society of Human Genetics annual meeting. Dr. Keegan has been an exam item writer for the American Board of Medical Genetics and Genomics, and is a member of the Board of Consulting Editors for *JCI Insight*. She was elected to serve as a member on the Medical School Advisory Committee for Appointments, Promotions, and Tenure from 2017-2020, and served as the chair from 2018-2019.

External Reviewers:

Reviewer A: "Her CV lists a number of research interests, but it is in the areas of the development of caudal malformations and the genetic disorders of sexual development (DSDs) that I am most familiar… Having a career long interest in this condition made be [sic] aware of those papers, and it was from there that I had first [sic] first-hand knowledge of her achievements in our field. Some recent papers on the DSDs in the special issue of the *American Journal of Medical Genetics, Part C* on DSDs in 2017 where she was a major contributor and senior author also illustrate her contributions to the field and her international reputation."

Reviewer B: "Dr. Keegan and her group have made impressive contributions to the better understanding of caudal malformations and the *in vivo* consequences of telomere dysfunction… Given the high quality of the journals in which these papers are published and the impact of her work, as well as the impressive results reported, I consider this an indication of her excellent scientific productivity… She has given a number of invited presentations at educational institutions and at professional meetings, and having attended some of these, I can attest to the high quality of her lectures."

Reviewer C: "Accordingly, Dr. Keegan has contributed significantly to her field- not only in service, education and clinical excellence but also in research. She is among the increasingly rare cadre of physician scientists who are so needed in translational research who has made a major impact in the fields of genetics of human gene disorders in general and more specifically, in the areas of disorders of sex differentiation and developmental biology (caudal malformations) and telomere biology. She has continued in more recent years (since her appointment to Associate Professor) to demonstrate continued scholarship and leadership."

Reviewer D: "…Dr. Keegan provides ample evidence that she is an excellent and active researcher. In addition, she provides abundant and important contributions to the discipline as evidenced by her serving on committees, as manuscripts reviewer, and other activities. She compares favorably with her peer group as evidenced by her election to notable societies

including the American Society for Clinical Investigation, the American Pediatric Society, and the Society for Pediatric Research. In fact, there is a shortage of individuals with her research and clinical expertise."

Reviewer E: "I am mostly familiar with Dr. Keegan's work on the Danforth short tail mouse, which she has studied for a number of years as a model of caudal regression in human patients… Her research in the area has led to solid gene-discovery publications in journals such as Human Molecular Genetics, Developmental Biology, and PLoS Genetics. Most recently she has shown, along with her collaborators, that the retrotransposon disruption of an enhancer in the Danforth mouse is associated with dysregulated Hedgehog signaling in early tailbud development. This is an important new mechanistic insight and I expect that Dr. Keegan will continue to steadily contribute to our understanding of this developmental dysregulation."

Reviewer F: "She has been productive, having co-authored approximately 25 peer-reviewed published papers since her promotion, ten as senior author, that are published in top-tier journals, including *Journal of Clinical Investigation*, *PLoS Genetics* and *Human Molecular Genetics*. Her approach is comprehensive, and her publications contain beautiful data. Consequently, several of her publications have had a high degree of impact in the field… She is recognized as an excellent investigator in human genetics."

Summary of Recommendations:
Dr. Keegan is a nationally and internationally recognized and accomplished physician-scientist who has made broad and enduring contributions in her field of research and in medical genetics clinical care. At Michigan Medicine, she has been extremely active in administrative leadership, research, service, and teaching. I am pleased, therefore, to recommend Catherine E.H. Keegan, M.D., Ph.D. for promotion to professor of pediatrics, with tenure, Department of Pediatrics, and professor of human genetics, without tenure, Department of Human Genetics, Medical School.

Marschall S. Runge, MD, PhD
Executive Vice President for Medical Affairs
Dean, Medical School

May 2020