Approved by the Regents May 21, 2015

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF MOLECULAR AND INTEGRATIVE PHYSIOLOGY
DEPARTMENT OF INTERNAL MEDICINE

Ken Inoki, M.D., Ph.D., assistant professor of molecular and integrative physiology, Department of Molecular and Integrative Physiology, and assistant professor of internal medicine, Department of Internal Medicine, Medical School, is recommended for promotion to associate professor of molecular and integrative physiology, with tenure, Department of Molecular and Integrative Physiology, and associate professor of internal medicine, without tenure, Department of Internal Medicine, Medical School [also being promoted to research associate professor, Life Sciences Institute].

Academic Degrees:

Ph.D.	1998	Shiga University of Medical Science, Otsu, Shiga, Japan
M.D.	1990	Shiga University of Medical Science, Otsu, Shiga, Japan

Professional Record:

2008-present	Assistant Professor of Molecular and Integrative Physiology and Assistant Professor of Internal Medicine, University of Michigan
2008-present	Research Assistant Professor, Life Sciences Institute, University of Michigan
2004-2008	Assistant Research Scientist, Life Sciences Institute, University of Michigan
1998-2001	Medical Instructor, Department of Nephrology, Shiga University of Medical Science, Otsu, Shiga, Japan

Summary of Evaluation:

Teaching: Dr. Inoki has participated in one MIP/Biochem/Pharmacology graduate student course (Biochem 591: Special Topics in Signal Transduction), in which he focuses on topics related to nutrient and growth factor sensing mechanisms. In this context, graduate students have generally rated him as 'excellent;' however, the proportion of students rating him as 'fantastic' increased over the past two years. The laudatory comments by the students include phrases such as "asked very insightful and engaging questions," "very knowledgeable," "very fair," and "thoughtful discussion." In addition, Dr. Inoki has repeatedly taught the M1 Renal medical student small group conference, where the students commented that he is knowledgeable and effective. He currently is teaching Biochem 552. Dr. Inoki has been a member of ten dissertation committees (four currently), five preliminary examination committees, and has mentored individuals in his lab, including post-doctoral fellows, visiting scholars, a master's student, and undergraduates. Two of his post-doctoral fellows are now assistant professors at the University of Tokyo. In all of these capacities, he has been a terrific and conscientious teacher and mentor.

Research: Since his appointment as assistant professor, Dr. Inoki published four high profile publications in top peer-reviewed journals including *Molecular Cell*, *Journal of Biological Chemistry*, and *Journal of Clinical Investigation*, either as first or last author. He is a very collaborative investigator who has since 2009, co-authored 17 additional publications emanating from the labs of

six other University of Michigan Medical School faculty and eight other investigators outside the university. He is a well-funded researcher, particularly given the current funding climate. Dr. Inoki is currently the principal investigator on a NIH R01 grant (which received a fundable score in competitive renewal) and a co-investigator on another R01 grant. He has recently submitted three additional proposals, two R01 grants and an American Diabetes Association grant. Dr. Inoki has a growing national and international reputation. He has established himself as one of the leaders in understanding how inappropriate activation of the mTOR pathway in glomerular podocytes causes podocyte dysfunction and diabetic nephropathy. He is also making mechanistic insights into mTOR mechanism of action. For example, he discovered that an mRNA-binding protein (LARP1) is a novel mTOR substrate that is involved in regulation of translation. He has 11 invited reviews or methods papers and has been an invited speaker at 10 national or international meetings, a NIH workshop and two presentations at Canadian universities. His research contributions were recently recognized by his membership in The American Society for Clinical Investigation.

Recent and Significant Publications:

Inoki K*, Mori H, Wang J, Suzuki T, Hong S, Yoshida S, Blattner SM, Ikenoue T, Rüegg MA, Hall MN, Kwiatkowski DJ, Rastaldi MP, Huber TB, Kretzler M, Holzman LB, Wiggins RC, Guan KL*: mTORC1 activation in podocytes is a critical step in the development of diabetic nephropathy. (*co-corresponding) *J Clin Invest* 121:2181-2196, 2011.

Yoshida S, Hong S, Suzuki T, Nada S, Mannan AM, Wang J, Okada M, Guan KL, Inoki K: Redox regulates mTORC1 activity by modulating the TSC1/TSC2-Rheb pathway. *J Biol Chem* 286:326251-326260, 2011.

Narita M, Young A, Arakawa S, Samarajiwa SA, Nakashima T, Yoshida S, Hong S, Berry LS, Reichelt S, Ferreira M, Tavaré S, Inoki K, Shimizu S, Narita M: Spatial Coupling of mTOR and Autophagy Augments Secretory Phenotypes. *Science* 332:966-970, 2011.

Suzuki T, Bridges D, Nakada D, Skiniotis G, Morrison SJ, Lin J, Saltiel AR, Inoki K*: Inhibition of AMPK catabolic action by GSK3. *Mol Cell* 50:407-419, 2013.

Hong S, Zhao B, Lombard DB, Fingar DC, Inoki K*: Crosstalk between sirtuin and mammalian target of rapamycin complex 1 (mTORC1) signaling in the regulation of S6 kinase 1 (S6K1) phosphorylation. *J Biol Chem* 289:13132-13141, 2014.

Service: Dr. Inoki is currently serving on the Cell and Molecular Biology (CMB) Ph.D. program committee, which can be a time-consuming committee, and has served on the CMB Recruitment Committee. On a national level, he has served as an ad hoc member on NIH study sections and is a reviewing editor for one of the top journals in the cell biology field, *Molecular Biology of the Cell.*

External Reviewers:
Reviewer A: "Dr. Inoki has given 1-2 invited presentations/year at national or international forums and this year was elected to membership in the American Society for Clinical Investigation. Since 2011 he has been a member of the NIH study section 'cellular and Molecular Biology of the Kidney' and he is a reviewing editor for Molecular Biology of the Cell. These circumstances attest to his recognition as an established investigator."

Reviewer B: "It is clear to me that Ken has really established a strong research program already supported by a recently renewed NIH grant focused on Diabetic Nephropathy with the potential for two more grants. Dr. Inoki's University of Michigan's academic contributions clearly extend beyond his own research efforts. I see that he is contributing to teaching of graduate and medical students. He is also mentoring postdocs and students in his laboratory. Ken is serving on the CMB program committee, and the dissertation and thesis committees of several students. Thus his contributions to the university are significant and important."

Reviewer C: "...Dr. Inoki's research program has been characterized by conceptual innovation, mechanistic rigor, and medical relevance. It is clear to me that his program is on a continued upward trajectory. At this stage of his career, he would certainly be awarded tenure in my institute."

Reviewer D: "...these two papers by Inoki were landmarks in the field, providing evidence for the mechanisms by which signaling pathways that monitor the availability of nutrients (Akt) or energy (AMPK) impact on a signaling pathway that regulates cell growth (mTORC1) and that is of critical importance in cancer."

Reviewer E: "...it is no doubt that Dr. Inoki has strong research ability in both basic cell biology and pathophysiology."

Summary of Recommendation:
Dr. Inoki is an outstanding candidate for promotion to associate professor, with tenure, based on his contributions on all missions: research and scholarly activities, education and mentoring, and service. His external letters of evaluation and his election to the American Society of Clinical Investigation are strongly supportive of his promotion, and affirm his international stature as a leading nephrology researcher. It is anticipated that he will continue to excel and grow his academic career at the University of Michigan, and to serve as a superb role model. Therefore, I enthusiastically support the promotion of Ken Inoki, Ph.D. to associate professor of molecular and integrative physiology, with tenure, Department of Molecular and Integrative Physiology, and associate professor of internal medicine, without tenure, Department of Internal Medicine, Medical School.

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

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