

Approved by the  
Regents  
May 21, 2015

PROMOTION RECOMMENDATION  
THE UNIVERSITY OF MICHIGAN  
MEDICAL SCHOOL  
DEPARTMENT OF MICROBIOLOGY AND IMMUNOLOGY

Philip D. King, Ph.D., associate professor of microbiology and immunology, with tenure, Department of Microbiology and Immunology, Medical School, is recommended for promotion to professor of microbiology and immunology, with tenure, Department of Microbiology and Immunology, Medical School.

Academic Degrees:

Ph.D.	1991	University College London, United Kingdom
B.Sc.	1986	University of Glasgow, Scotland

Professional Record:

2006-present	Associate Professor of Microbiology and Immunology, University of Michigan
2002-2006	Assistant Professor of Microbiology and Immunology, University of Michigan
1998-2002	Assistant Professor, Immunology in Medicine, Weill Medical College of Cornell University
1997-2002	Assistant Scientist, Hospital for Special Surgery, Weill Medical College of Cornell University

Summary of Evaluation:

Teaching: Dr. King serves as a dedicated and capable teacher in department courses for medical and graduate students and for trainees and research investigators in his lab. Since his last promotion in 2006, he has been a lecturer and course director for M&I 640 (Molecular and Cellular Immunology, 20 students per year), M&I 641 (Advanced Immunology, seven students per year) and the M1 medical school course in immunology (180 students per year). For all three courses, he developed or helped to develop new course curricula to address changing pedagogical needs of the Medical School and the immunology graduate program. Since his last promotion, he trained four predoctoral students and four post-doctoral students in his lab, as well as two M1 medical students and two undergraduates who performed honors thesis research. Trainees from his lab obtained post-doctoral or faculty positions in prestigious institutions. He also served on 21 pre-doctoral qualifying exam committees, 13 pre-doctoral thesis advisory committees and a thesis committee for a student at the University of Texas. He served as chair of the Graduate Studies Committee of the department from 2007 to 2010. In addition to the graduate program in Microbiology and Immunology, he was a member of the training faculty for the Graduate Program in Immunology and the Cellular Biotechnology Training Program.

Research: Dr. King's laboratory studies intracellular signaling pathways that regulate cellular growth, proliferation, survival, and differentiation. They also study how inherited and acquired mutations in genes that encode different signaling pathway components result in disease. A longstanding focus of interest was the mechanisms of signal transduction in cells of the immune system. More recently, he has turned to signaling mechanisms in blood and lymphatic vascular endothelial cells and cells that regulate bone, i.e. osteoblasts, chondrocytes and osteoclasts. His lab's primary approach entails conditional gene targeting in mice by homologous recombination in embryonic stem cells. This permits an understanding of receptor signal transduction in the context of the whole animal. Since his last promotion, Dr. King's laboratory has generated seven different novel conditional knockout or knockin mouse strains and twenty-plus different compound mutant mouse strains derived thereof. Most of the genes that have been targeted encode regulators of the ubiquitous Ras signaling pathway, including non-receptor protein tyrosine phosphatases, intracellular adapter proteins and Ras GTPase-activating proteins that act upstream and downstream of Ras. The phenotypes that have emerged in these mice point to the complexity of mechanisms by which Ras activation is controlled and how these mechanisms vary between different cell types. Furthermore, several of the generated mouse strains have emerged as important models of inherited genetic diseases in man that have yielded insights into mechanisms of disease pathogenesis, including systemic lupus erythematosus, syndromic diseases such as Noonan syndrome and LEOPARD syndrome, vascular anomalies such as capillary malformation-arteriovenous malformation and hematological cancers such as T cell acute lymphoblastic leukemia. In some instances, phenotypes in mice have led to novel insights about corresponding human disease that had not been appreciated beforehand. A prominent example is the discovery of lymphatic vessel abnormalities in inducible RASA1-deficient mice that pointed to the existence of similar abnormalities in humans with RASA1 mutations. The current emphasis of the lab concerns how the Ras pathway regulates lymphatic and blood vessel development and function in health and disease. Dr. King's research program has earned international recognition. Since his last promotion in 2006, he has published 30 papers (19 as first or senior author) in high quality journals, and three book chapters. His research was supported by American Heart Association grants and two R01 NIH grants, and is currently supported by an R21 grant, entitled, "Random Monoallelic Expression and Human Disease" (through January, 2106). Additionally, he has just received a priority score of 1%-ile on his latest R01 submission. Since 2006, he has given six seminars at UM and seven invited lectures at national and international forums (England, Italy, China).

#### Recent and Significant Publications:

Marti F, Garcia G, Lapinski PE, MacGregor JN, King PD: Essential role of the T cell-specific adapter protein in the activation of the LCK protein tyrosine kinase in peripheral T cells. *J Exp Med* 203:281-287, 2006.

Bauler TJ, Hughes ED, Arimura Y, Mustelin T, Saunders TL, King PD: Normal TCR signal transduction in mice that lack catalytically-active PTPN3 protein tyrosine phosphatase. *J Immunol* 178:3680-3687, 2007.

Bauler TJ, Kamiya N, Lapinski PE, Langewisch E, Mishina Y, Wilkinson JE, Feng GS, King PD: Development of severe skeletal defects in induced SHP-2-deficient adult mice: a model of skeletal malformation in humans with SHP-2 mutations. *Dis Model Mech* 4:228-239, 2011.

Lapinski PE, Qiao Y, Chang C-H, King PD: A role for p120 RasGAP (RASA1) in thymocyte positive selection and survival of naïve T cells in mice. *J Immunol* 187:151-163, 2011.

Lapinski PE, Kwon S, Lubeck BA, Wilkinson JE, Srinivasan S, Sevic-Muraca E, King PD: RASA1 maintains the lymphatic vasculature in a quiescent functional state in mice. *J Clin Invest* 122:733-747, 2012.

Service: Since his last promotion, Dr. King has served on numerous committees at UM and for national and international organizations. For the department, he was chair of the Graduate Studies Committee and a member of Appointments, Promotions and Awards Committee. For the Medical School, he was a member of the Admissions Committee and Operating Committee for PIBS, the Preliminary Exam Committee and the Admissions Committee for the Immunology Graduate Program, and the Component 1-2 Curriculum Committee for Medical Student Teaching. He served on study sections for the American Heart Association (2007-2010), the NIH (ad hoc for four study sections, 2009-2012), the US-Israel Binational Science Foundation and the French National Research Agency. At the University of Michigan, he reviewed grant applications for the Burroughs-Wellcome Fund Pathogenesis of Infectious Disease and for the Biomedical Research Council. He reviewed manuscripts for 16 journals, and serves on the editorial boards of the Alliance for Cellular Signaling, the Human Protein Resource Database, *ISRN Immunology Journal* and the *American Journal of Clinical and Experimental Immunology*.

External Reviewers:

Reviewer A: "...what is most impressive in my opinion is that Dr. King has made substantial and impactful scientific contributions in several diverse fields that are beyond his classical training...I can think of few scientists who have the intellectual dexterity, perseverance and motivation to venture into uncharted scientific disciplines and succeed! Therefore, in this regard, I feel strongly that Dr. King has not only met, but exceeded, the expectation of a full professor by having expanded his research contributions to new and innovative areas that have garnered wide-spread international recognition for their interdisciplinary scope and breadth."

Reviewer B: "Dr. King has maintained or increased his international reputation through his move into this new area, with invitations to present at international meetings and seminars in Europe and Asia. His advice has also been sought on funding decisions in the US and abroad. Importantly, he has served on study sections that review grants in the cardiovascular diseases area, evidence that he has become a recognized expert in this area."

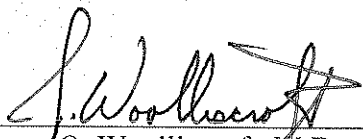
Reviewer C: "...Dr. Philip King is an outstanding scientist who has made important contributions to immunology and signal transduction and established an international reputation. He is also likely to make important contributions to the study of signaling molecules in lymphangiogenesis and various human diseases."

Reviewer D: "It is fair to describe Dr. King's work investigating RASA1 in blood vascular malformations and its role in lymphatic vascular development as a seminal advance in the field of blood and lymphatic vascular biology."

Reviewer E: "His papers are a mix of primary papers from his laboratory and collaborative papers. They are all data intensive, good quality papers in journals of high and very high profile in Immunology and Science, including papers in *Nature Medicine*, *Science Signalling*, *Journal of Experimental Medicine*, *JCI* and *PNAS*."

Summary of Recommendation:

Dr. King has distinguished himself as an outstanding researcher and colleague who has earned the respect of his peers in the field and the admiration of his Michigan colleagues. He continues to apply state-of-the-art molecular and genetic technologies to make important discoveries related to receptor-mediated signal transduction. Notably, he has, since his last promotion, developed a new area of expertise which is already garnering international recognition. He has made outstanding contributions in research, teaching and service, and he shows great promise for continued success as a scholar. I wholeheartedly recommend Philip D. King, Ph.D. for promotion to professor of microbiology and immunology, with tenure, Department of Microbiology and Immunology, Medical School.



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James O. Woolliscroft, M.D.

Dean

*Lyle C. Roll Professor of Medicine*

May 2015