PROMOTION RECOMMENDATION UNIVERSITY OF MICHIGAN MEDICAL SCHOOL DEPARTMENT OF PHARMACOLOGY

Roger K. Sunahara, Ph.D., associate professor of pharmacology, with tenure, Department of Pharmacology, Medical School, is recommended for promotion to professor of pharmacology, with tenure, Department of Pharmacology, Medical School.

Academic Degrees:

Ph.D. 1993 University of Toronto B.Sc. 1988 University of Toronto

Professional Record:

2008-present Associate Professor of Pharmacology, University of Michigan 2001-2008 Assistant Professor of Pharmacology, University of Michigan

1998-2001 Assistant Professor (Research) of Pharmacology, University of Texas

Southwestern Medical Center

Summary of Evaluation:

Teaching: Dr. Sunahara has made major contributions to teaching in the department, the school, and the university. He has been invited and has given numerous lectures in his field of interest. He has been involved in teaching Pharmacology 660, CMB 530, Chembio 602, Biophysics 801, Med. Chem 419, Pharmacology 601, Chembio 501, and Biophysics 801 and is course director in Pharmacology 619 (Structural Basis for Drug Action). Dr. Sunahara is recognized as an excellent communicator who is both energetic and interactive with peers and students alike. His lectures are described by faculty and students as outstanding, insightful and well prepared. Dr. Sunahara has proven to be a superior teacher. He has also excelled in graduate student mentoring of pre- and post-doctoral fellows. He has supervised 10 Ph.D. candidates and six post-doctoral fellows.

Research: Dr. Sunahara is a nationally recognized expert in signal transduction mechanisms who has made significant contributions to the structural elucidation of the interaction between G proteins and G protein-coupled receptors (GPCRs). He is recognized for his superb talents in biochemistry, DNA technology, molecular biology, protein engineering, protein structure, protein crystallography and pharmacology, and uses these skills to make new and challenging discoveries. He has emerged as a leader in the field and has made seminal contributions to our understanding of the structure and function of GPCRs. Recently, his research group discovered the value of using HDL particles to study GPCRs in a well-defined and controlled membrane system and applied this technology to quantify the signaling activities of the unambiguously defined β2-adrenergic receptor and rhodopsin monomers. His work has provided clear insight into the importance, function, and regulation of GPCR oligomerization. He has also been a key collaborator with many top-tier scientists and was an important collaborator in the work led by Dr. Brian Kobilka to solve the structure of a nanobody-activated state of the β2-adrenergic

receptor and the structure of this receptor bound to a high affinity agonist. This collaboration resulted in three papers in 2011 that describe the mechanism of activation of Gs by this GPCR. Two of these papers were published in the same issue of Nature with Dr. Sunahara as corresponding or co-corresponding author and one in PNAS, again with Dr. Sunahara as corresponding author. The publication of these three papers last year had a major impact on the field. The huge advances for our understanding of the mechanisms of hormone action at the atomic level made from work with Dr. Brian Kobilka, co-recipient of the 2012 Nobel Prize in Chemistry, and his colleagues are widely recognized. Over the period from 2007 to 2012, Dr. Sunahara has 18 publications with Dr. Kobilka, primarily in Nature or PNAS, and Dr. Sunahara is either the corresponding or co-corresponding author on most of these publications. Dr. Sunahara has a total of 87 peer-reviewed publications with an h-index of 34 and a total of more than 7800 citations with almost 800 already in 2012. He has also contributed chapters to nine highly regarded books over the past several years and his work on G protein signaling and adenylyl cyclase action has led to more than 100 national or international invitations to present his research and other peer institutions have actively recruited him. He has also been successful in that his research has been recognized by his success in obtaining assorted extramural funding from NIH and various corporations.

Recent and Significant Publications:

Whorton MR, Bokoch MP, Rasmussen SGF, Huang B, Zare RN, Kobilka B, Sunahara RK: A monomeric G protein coupled receptor efficiently couples to its G protein. *Proceeding of the National Academy of Sciences* 104:7682-7687, 2007.

Whorton MR, Jastrzebska B, Park PS-H, Fotiadis D, Engel A, Palczewski K, Sunahara, RK: Efficient coupling of transducin to monomeric rhodopsin in a phospholipid bilayer. *Journal of Biological Chemistry* 283:4387-4394, 2008.

Yao XJ, Vélez Ruiz G, Whorton MR, Rasmussen SG, DeVree BT, Deupi X, Sunahara RK (Cocorresponding), Kobilka BK: Effect of ligand efficacy on the formation and stability of a GPCR-G protein complex. *Proceeding of the National Academy of Sciences* 106(23):9501-9506, 2009.

Rasmussen SGF, DeVree BT (equal first), Zou Y, Kruse AC, Chung KY, Thian T-S, Thian F-S, Chae PS, Pardon E, Calinski D, Mathiesen JM, Shah TSA, Lyons JA, Caffrey M, Gellman SH, Steyaert J, Skiniotis G, Weis WI, Sunahara RK (Co-corresponding), Kobilka BK: Crystal structure of the β2 adrenergic receptor-Gs protein complex. *Nature* 477:549-555, 2011.

Chung KY, Rasmussen SGF, Liu T, Li S, DeVree BT, Chae PS, Calinski D Kobilka BK, Woods Jr VL, Sunahara RK: β2 adrenergic receptor-induced conformational changes in the heterotrimeric G protein Gs. *Nature* 477:611-615, 2011.

<u>Service</u>: Dr. Sunahara actively participates throughout the university on numerous committees, conferences, and research partnerships. He currently serves on the University's Macromolecular Structure Initiative Committee, the Single Molecule Spectroscopy Steering Committee, and the Protein Structure, Design and Dynamics Committee. He has coordinated graduate admissions both for the Chemical Biology Program and the Department of Pharmacology. Within the Department of Pharmacology, he has served on numerous thesis and prelim committees, and

currently serves on the Department Awards Committee, which he chairs, and Seminar Committees. Dr. Sunahara also has very high national and international visibility. He has served as an ad hoc reviewer for many top tier scientific journals (*Biochemistry, Molecular Pharmacology, Journal of Biological Chemistry, Journal of Cell Biology, Journal of Neurochemistry, Journal of Neuroscience, EMBO Journal*, and Proceedings of the National Academy of Sciences) and is presently an editorial board member for the Journal of Biochemistry. He was the co-organizer of the GPCR Workshop, Honolulu, Hawaii, in 2010 and is co-organizer of the G protein-Coupled Receptors, Experimental Biology in Washington, D.C., in April 2013. He also has served as an ad hoc reviewer for several NIH study sections including NIGMS and NIDDK and also for CIHR (Canadian Institute of Health Research) and study section for Burroughs Wellcome. More recently, he has been an ad hoc reviewer for NIH study section MIST and recently was asked to serve as a permanent member. He has received 62 invitations to speak at national/international symposia since his promotion in 2008.

External Reviewers:

Reviewer A: "It is obvious from his list of publications that Roger is a stellar independent investigator. His work is published in the best journals and his papers have a significant impact on the scientific community and many are landmarks in the field....His work was crucial to solve long sought questions about the conformational changes of both receptors and heterotrimeric G proteins underlying their activation processes."

Reviewer B: "I would hope that your APT committee would not need more than a one liner endorsement to make this very obvious decision...Interestingly, having served for several years on the Endowed Chair Committee at our institution, Roger's H index of 34 [is] similar to that of individuals that we sometimes evaluate for endowed chairs....There is no doubt that Dr. Sunahara would be considered an exceptional candidate for promotion to Full Professor here [at my institution]...and more than likely at any institution in this country."

Reviewer C: "...Dr. Sunahara has developed a first-rate independent research program that pursues front of the field questions with ambitious goals. I have no doubt that he will continue to flourish in his studies on structure/function of GPCR, and he will expand his research program into exciting new areas....Roger Sunahara is a natural leader who will enormously help the science of other independent investigators with whom he interacts. His creativity, outstanding scientific instincts, and high values will keep him well funded."

Reviewer D: "His work has always been excellent, creative in its approaches and very rigorous...it is now clear that Sunahara has become one of the true leaders in understanding the molecular basis for signal transduction by heterotrimeric G protein coupled systems at the atomic level. He would certainly merit promotion to Professor at my institution."

Reviewer E: "...his recent synergistic collaborative work with Dr. Kobilka on the β -adrenergic receptor structure and its complex with Gs will be truly transformative to the field. It represents a Holy Grail in G protein signaling and has been the pursuit of many groups in both academia and the pharmaceutical industry for two decades."

Reviewer F: "In sum, based on his original, creative, and focused research, Dr. Sunahara has established himself as one of the world's leaders in his field. I have no doubt that Dr. Sunahara will continue making fundamental contributions to his chosen field of research."

Summary of Recommendation:

Dr. Sunahara has made major contributions to his field in understanding the structure and mechanism of activation of G protein coupled receptors (GPCRs) and the elucidation of the first structure of a GPCR activating a G protein. He has also made significant contributions to a number of departmental and university service activities, and is highly sought after for service opportunities on a national scale. I fully expect that Dr. Sunahara will continue to receive national recognition and that a bright future lies ahead for him. Without reservation, I enthusiastically recommend Roger K. Sunahara, Ph.D. for promotion to professor of pharmacology, with tenure, Department of Pharmacology, Medical School.

James O. Woolliscroft, M.D.

Dean

Lyle C. Roll Professor of Medicine

May 2013