

May 17, 2007

PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN MEDICAL SCHOOL
DEPARTMENT OF PHARMACOLOGY

Lori L. Isom, 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.	1987	Vanderbilt University
A.B.	1982	Washington University

Professional Record:

2001-Present	Associate Professor of Pharmacology, University of Michigan
1995-2001	Assistant Professor of Pharmacology, University of Michigan
1993-1995	Lecturer, Department of Pharmacology, University of Washington, Seattle

Summary of Evaluation:

Teaching: Dr. Isom is a very effective teacher and has participated in a number of department courses such as Pharmacology 210 (Antibiotics), Pharmacology 500 (Principles of Pharmacology), Pharmacology 501 (Advanced Topics in Pharmacology, Pharmacology 502 (Introduction to Scientific Communication), Pharmacology 600 (Independent Study in Pharmacology), Dental Pharmacology 602, and Molecular Neuropharmacology 615. In addition, she has lectured in courses run by the Neuroscience Program, Physiology, Biology, and Cell Biology. In each of these courses, the major theme of her teaching has been that of ion channels or anesthetic action. The Course Directors (Drs. Uhler, Neubig, Ernst, and Samuelson) have lauded her teaching skills and Dr. Isom has received strong positive feedback from students. One course, Introduction to Scientific Communication, was initiated by Dr. Isom and is designed to instruct students and postdoctoral fellows in scientific writing, hypothesis development, and experimental design. Students are instructed in how to prepare and evaluate a grant application and the course concludes with a mock NIH-style Study Section in which students evaluate each other's proposals. Additionally, Dr. Isom has successfully mentored three graduate students, 18 undergraduates, and nine postdoctoral fellows in her laboratory. Four of her postdoctoral fellows have obtained positions in academia, while three others have gone on to positions in industry.

Research: Dr. Isom has successfully established herself as an independent researcher with her work on ion channels, especially the beta subunits of the voltage-gated sodium channel. The focus of Dr. Isom's research is the study of sodium channel structure and function (channel gating, voltage dependence of inactivation/activation, plasma membrane expression and localization of Na⁺ channels, and the functioning of Nav β subunits in the regulation of

cardiac Nav channels). She continues to be highly productive and since 2001, lists over 20 peer-reviewed publications in a number of high quality, high visibility journals such as *Cardiovascular Research*, *Journal of Biological Chemistry*, *American Journal of Physiology*, *Journal of Neurochemistry*, and *Journal of Neuroscience*. A major portion of her work is on the potential role played by β subunits as cell adhesion molecules and she is recognized nationally and internationally as an expert in the biological roles of auxiliary β subunits of voltage-gated Na^+ channels in the brain and heart.

Dr. Isom effectively makes use of a combination of electrophysiology, biochemistry, immunocytochemistry, and cell biology approaches combined with the generation of genetic animal models to address key specific questions regarding the function of β subunits in Na^+ channel function, both *in vivo* and *in vitro*. The work is very high quality, novel and makes a significant contribution to our understanding of basic mechanisms of Na^+ channel function and expression. Her contribution to the understanding of ion channels as multi-functional macro-molecular complexes has been seminal and trend-setting. Moreover, the results obtained could provide the basis for future therapeutic interventions in epilepsy, ataxia, and multiple sclerosis. Dr. Isom also continues to be successful in securing extramural funding, including funding from the NIH, the National Multiple Sclerosis Society, Pfizer Global Research, and Wyeth Pharmaceuticals.

Recent and Significant Publications:

Lopez-Santiago LF, Pertin M, Morisod X, Chen C, Hong S, Wiley J, Decosterd I, Isom LL: Sodium channel $\beta 2$ subunits regulate tetrodotoxin-sensitive sodium channels in small dorsal root ganglion neurons and modulate the response to pain. *J Neuroscience* 26:7984-7994, 2006.

Davis TH, Chen C, Isom LL: Sodium channel $\beta 1$ subunits promote neurite outgrowth in cerebellar granule neurons. *J Biological Chemistry* 279:51424-51432, 2004.

Chen C, Westenbroek RE, Xu X, Edwards CA, Sorenson DR, Chen Y, McEwen DP, O'Malley HA, Bharucha V, Meadows LS, Knudsen GA, Vilaythong A, Noebels JL, Saunders TL, Scheuer T, Shrager P, Catterall WA, Isom LL: Mice lacking sodium channel $\beta 1$ subunits display defects in neuronal excitability, sodium channel expression, and nodal architecture. *J Neuroscience* 24:4030-4042, 2004.

Chen C, Bharucha V, Chen Y, Westenbroek RE, Brown A, Malhotra JD, Jones D, Avery C, Gillespie III PJ, Kazen-Gillespie KA, Kazarinova-Noyes K, Shrager P, Saunders TL, Macdonald RL, Ransom BR, Scheuer T, Catterall WA, Isom LL: Reduced sodium channel density, altered voltage dependence of inactivation, and increased susceptibility to seizures in mice lacking sodium channel beta 2-subunits. *PNAS* 99:17072-17077, 2002.

Malhotra JD, Koopmann MC, Kazen-Gillespie KA, Fettman N, Hortsch M, Isom LL: Structural requirements for interaction of sodium channel $\beta 1$ subunits with ankyrin. *J Biological Chemistry* 277:26681-26688, 2002.

Service: Dr. Isom actively participates on a number of committees both in the Medical School and in the Department. Since January 2006, she has served as Associate Director of the Program in Biomedical Sciences (PIBS). She also serves on the PIBS Admissions Committee, the PIBS Operating Committee, and the PIBS Curriculum Committee, the Human Genetics Predoctoral Training Grant Executive Committee, and has served on the Graduate Program in Cellular and Molecular Biology Program Committee. Within the Department of Pharmacology, she has served on the Advisory, Graduate Program, Graduate Student Recruitment, Internal Review, and Faculty Awards committees. She also planned and organized the Department of Pharmacology Annual Retreat for several years, and recently was assigned the task of establishing a career development program for postdoctoral fellows within the Medical School. Dr. Isom also has outstanding national and international visibility. She has served as an *ad hoc* reviewer for many top tier scientific journals and for several NSF Study Sections, the NIH, the National Multiple Sclerosis Society, and the Wellcome Trust. She has organized and chaired symposia at the Experimental Biology meetings, the University of Michigan, and most recently the Great Lakes Glial Meeting. She has received more than 32 invitations to speak at national/international symposia (including the American Heart Association, the Heart Rhythm Society, Cold Spring Harbor, the Jackson Laboratory Neurogenetics Conference V, the International Association for the Study of Pain Meeting, and a number of prestigious universities such as Harvard, Emory and Columbia). These events have been highly successful and provide further evidence of Dr. Isom's recognition in her field and overall commitment to it.

External Review:

Reviewer A: "Let me begin then by stating simply that I think that Dr. Isom is an exceptional individual and a truly first rate scientist. She is clever, thoughtful, critical and creative, and she is internationally recognized for her contributions to our present understanding of the molecular physiology of neuronal Nav channels."

Reviewer B: "Dr. Isom's work shows originality and has high significance for the ion channel field. She is held in high regard among her peers, and is nationally and internationally recognized. Her accomplishments to date leave no doubt that her service to the community and her scholarly achievements will continue."

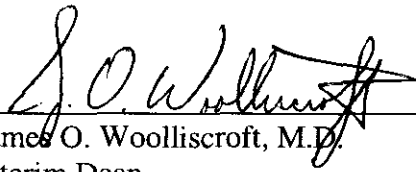
Reviewer C: "Her trajectory as a productive independent scientist is clearly upward despite the large number of contributions she has already made....Her presence strengthens both the Department of Pharmacology in particular and the University of Michigan in general."

Reviewer D: "Her work on ion...channels has consistently been highly original and at the cutting edge. Her contribution to the understanding of channels as multifunctional macro-molecular complexes has been seminal and trend-setting....We simply would give our right arm to be able to employ someone like Lori Isom in our department! Michigan should feel very lucky to have her."

Reviewer E: "Based upon my experience in...faculty search committees, Dr. Isom would be highly qualified for the position of a chairman for a department of physiology or biochemistry or pharmacology in...The evaluation of her scientific record and teaching experience would rank her without doubt among the best candidates."

Summary of Recommendation:

Dr. Isom has established a robust, high quality research program that attracts substantial extramural support and is an important resource for the training of undergraduate, graduate, and postdoctoral students. She is held in very high esteem by her colleagues within the Department and Medical School as well as by scientists throughout the country. She has developed a significant national and international visibility, her teaching and administrative skills are exemplary, and she makes significant contributions to the functioning of the Department and the Medical School. I enthusiastically support her promotion to Professor of Pharmacology.



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

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