PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN MEDICAL SCHOOL
DEPARTMENT OF MOLECULAR AND INTEGRATIAVE PHYSIOLOGY
DEPARTMENT OF INTERNAL MEDICINE
DEPARTMENT OF PHARMACOLOGY

Richard M. Mortensen, M.D., Ph.D., Associate Professor of Molecular and Integrative Physiology, with tenure, Department of Molecular and Integrative Physiology, Associate Professor of Internal Medicine, without tenure, Department of Internal Medicine, and Associate Professor of Pharmacology, without tenure, Department of Pharmacology, Medical School, is recommended for promotion to Professor of Molecular and Integrative Physiology, with tenure, Department of Molecular and Integrative Physiology, Professor of Internal Medicine, without tenure, Department of Internal Medicine, and Professor of Pharmacology, without tenure, Department of Pharmacology, Medical School.

Academic Degrees:

M.D.	1984	Cornell University Medical College
Ph.D.	1983	The Rockefeller University
B.S.	1976	Pennsylvania State University

Professional Record:

2002-Present	Associate Professor of Pharmacology, University of Michigan
2000-Present	Associate Professor of Molecular and Integrative Physiology and Associate Professor of Internal Medicine, University of Michigan
1992-2000	Assistant Professor of Medicine, Harvard Medical School
1990-1992	Instructor in Medicine, Brigham and Women's Hospital, Boston

Summary of Evaluation:

Teaching: Dr. Mortensen serves as block coordinator and presents 8-12 hours of material annually in the M1 Endocrine Block. This is a major teaching responsibility for which he has received excellent reviews from both students and the M1 year coordinator. His student evaluations from the last three years have fallen in the 3.14-3.48 range on a scale of 1 to 5 (best). Dr. Mortensen also has presented other small group conferences including renal, musculoskeletal, and reproductive physiology to M1 students. He has also presented material on nutritional assessment for the over weight/obese patient to M2 students. With regard to graduate student teaching, he has presented material in Organogenesis of Complex Systems (CMB 683) where he has covered in various years organogenesis of the heart, organogenesis of the pancreas, and most recently, stem cells and organogenesis. In the most recent year, 13 out of 14 students rated his teaching in this course as excellent or outstanding. He has also taught in Integrative Genomics (Physiology 555) where he presented material on transgenic mouse techniques, in Cardiovascular Pharmacology (Pharmacology 752), and

most recently, in Special Topics in Signal Transduction (Physiology 591) where students gave him an overall evaluation of excellent. In the laboratory, he has supervised thesis research for three Ph.D. students, two of whom have received their degrees. He has also supervised several additional recent PIBS rotations and a medical student conducting summer research. In addition, he has served on 18 preliminary exam committees and five other thesis committees.

Research: Dr. Mortensen's research deals with the pathophysiology of cardiovascular disease, obesity and diabetes. He focuses on the role of signal transduction pathways particularly heterotrimeric G proteins and transcription factors of the PPAR family. In his work he uses both embryonic stem cells and transgenic animals. In his early work he developed a widely used method to produce knockout cell lines by homologous recombination. He has been a pioneer in the targeted disruption of G protein subunits and the resultant effects on cardiac physiology, and has studied these mice both in his own laboratory and in collaborations throughout the country. Subsequently, he turned his attention to PPARγ and was the first to produce knockout embryonic stem cell lines. With Bruce Spiegelman's laboratory, he showed that deletion of PPARγ stopped differentiation of ES cells to adipocytes. He has defined an interesting phenotype in mice with cardiac-specific deletion of PPARγ showing that they develop spontaneous cardiac hypertrophy. Most recently, he developed a novel method to overcome the embryonic lethality of mice lacking systemic PPARγ and showed that they develop insulin resistance, hypotension and lipodystrophy. This work was published in the *Journal of Clinical Investigation* (2007) and has attracted considerable attention. His research has led to 47 original research publications and 16 chapters and reviews. He has been successful at competing for research grants and has held multiple grants from the NIH as well as grants from the American Heart Association and the American Diabetes Association. Currently, he holds two NIH R01 grants and is a co-investigator on another faculty member's NIH grant. As evidence of his expertise and scientific stature, he has been asked to serve on several NIH grant panels and has received an Established Investigator Award from the American Heart Association. Since 2005, he has been invited to give seven presentations on his research at other institutions.

Recent and Significant Publications:

Duan SZ, Ivashchenko C, Whitesall S, D'Alecy LG, Vinson C, Gonzalez F, Mortensen RM: Hypotension, lipodystrophy, and insulin resistance in generalized PPAR-gamma deficient mice rescued from embryonic lethality *J Clin Invest* 117 (3):812-822, 2007.

Ivashchenko C, Duan SZ, Usher M, Mortensen RM: PPAR-γ knockout in pancreatic epithelial cells abolishes the inhibitory effect of Rosiglitazone on cerulein-induced acute pancreatitis. *Am J Physiol: Gastrointestinal and Liver Physiology* 293:G319-G326, 2007.

Duan SZ, Russell MW, Milstone DS, Mortensen RM: Cardiomyocyte-specific knockout and agonists of PPAR-γ both induce cardiac hypertrophy in mice. *Circulation Res* 97: 372-379, 2005.

Jain M, Lim CC, Nagata K, Davis VM, Milstone DS, Liao R, Mortensen RM: Targeted inactivation of Galpha(i) does not alter cardiac function or beta-adrenergic sensitivity. *Am J Physiol: Heart Circ Physiol* 280:H569-H575, 2001.

Nagata K, Ye C, Jain M, Milstone DS, Liao R, Mortensen RM: Galpha(i2) but not Galpha(i3) is required for muscarinic inhibition of contractility and calcium currents in adult cardiomyocytes. *Circulation Res* 87:903-909, 2000.

Service: In the Department of Molecular and Integrative Physiology, Dr. Mortensen has served on the Graduate Committee, the Space Committee, and the Steering Committee for the Center for Integrative Genomics. In the Medical School he serves on the Pharmacological Sciences Training Program Biology Track Committee, the Steering Committee for Stem Cell Research, and on the MDRTC Scientific Advisory Council. He has also been a significant contributor to the Organogenesis Program. Recently, he was elected to a three-year term on the Medical School Curriculum Policy committee. Outside the University, he has provided service on NIH grant reviews as noted earlier and has reviewed grants for Takeda Pharmaceuticals. He also reviews manuscripts for a number of scientific journals.

External Review:

Reviewer A: "Dr. Mortensen is highly regarded in the fields of G protein and PPAR biology and physiology. He was a pioneer in the targeted disruption of G protein subunits, and he has used his expertise at gene targeting and blended it with a superb ability to analyze cardiac phyisology. His work with PPARγ is also highly influential, and the role of PPARγ in adipose differentiation and cardiac growth is extremely important. In my opinion, Dr. Mortensen's finding that PPARγ activity is required for adipose differentiation and vascular resistance are seminal advances in the field."

Reviewer B: "In 2005, the Mortensen laboratory defined an interesting phenotype in mice with cardiac-specific ablation of PPARγ. In my opinion, this latter piece of work is his most important contribution. More recently, using a clever genetic rescue strategy, the Mortensen laboratory found that PPARγ null mice are lipodystrophic and hypotensive (*JCI*, 2007). This is interesting and begins to reveal a mechanism for the known link between alterations in systemic lipid metabolism (e.g., lipodystrophy and Metabolic Syndrome) and hypertension."

Reviewer C: "...Dr. Mortensen's unique background in biochemistry, molecular biology, basic and clinical endocrinology, and cardiovascular physiology has allowed him to use his unique talents to create and then advance this important field. In particular, his work on PPAR knockouts and cardiomyocyte biology is truly unique and important."

Reviewer D: "...Dr. Mortensen is an outstanding scientist, contributing many seminal contributions to his field. He is heavily involved in teaching, peer-review and service to his university. He embodies those talents, which contribut to making him an excellent academic faculty member. I highly recommend him for this important promotion."

Reviewer E: "Not surprisingly, Mortensen's research accomplishments have been rewarded by publications in excellent journals, solid research funding, membership in study sections and review panels, and a highly regarded reputation. I am certain that his laboratory is an ideal environment for trainees in molecular physiology and the his mentorship provides thoughtful, considered, advice and wisdom to his trainees."

Summary of Recommendation:

Dr. Richard Mortensen has developed a reputation as a leading researcher in the use of mouse models to study cardiac and metabolic function and is highly regarded in the fields of G protein and PPAR biology. He is an important contributor to medical and graduate student teaching, and to the stem cell research effort at Michigan. I am pleased to recommend that he be promoted to the rank of Professor, with tenure, in the Department of Molecular and Integrative Physiology, and Professor, without tenure, in the Department of Internal Medicine and the Department of Pharmacology.

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

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