

PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF PEDIATRICS AND COMMUNICABLE DISEASES
DEPARTMENT OF PATHOLOGY

Steven W. Pipe, M.D., associate professor of pediatrics and communicable diseases, with tenure, Department of Pediatrics and Communicable Diseases, and associate professor of pathology, without tenure, Department of Pathology, Medical School, is recommended for promotion to professor of pediatrics and communicable diseases, with tenure, Department of Pediatrics and Communicable Diseases, and professor of pathology, without tenure, Department of Pathology, Medical School.

Academic Degrees:

M.D.	1989	University of Toronto
B.S.	1985	University of Toronto

Professional Record:

2007-present	Associate Professor of Pathology, University of Michigan
2004-present	Associate Professor of Pediatrics and Communicable Diseases, University of Michigan
1998-2004	Assistant Professor of Pediatrics and Communicable Diseases, University of Michigan
1996-1998	Lecturer, Department of Pediatrics and Communicable Diseases, University of Michigan

Summary of Evaluation:

Teaching: Dr. Pipe has broad exposure to learner categories at multiple levels throughout the University of Michigan. His most important educational contributions include curriculum design and development including an innovative clinical research fellowship in hemostasis and thrombosis that has already mentored two pediatric coagulation specialists, one of whom leads the coagulation program at Duke University. He has also developed curriculum to support the M2 hematology sequence, the Dental School IMS program, the hematopathology and the internal medicine/hematology fellowship programs. He has served as the fellowship director for the pediatric hematology and oncology program that recruits nationally and has maintained a productive NIH T32 training grant in molecular hematology. Seventy-seven percent of the fellows trained in this environment hold academic faculty positions around the country and 45% have successfully competed for extramural funding. He has mentored annually a number of students in the UROP and summer research opportunity training programs. Several of his trainees have been recipients of research awards and a number of these students have pursued training in graduate or medical school. On the wards, he has been consistently recognized as an excellent teacher by pediatric residents and medical students rotating on the hematology oncology and coagulation clinical services and this past year he was awarded a top teacher award from the pediatric housestaff and medical students.

Research: Dr. Pipe's basic science research has great significance in the field of pediatric hematology. His laboratory studies the biology of the factor VIII clotting protein. This protein, when deficient, is the cause of hemophilia, a devastating bleeding disorder of childhood. The over-arching goal of Dr. Pipe's research is to develop a biological therapeutic that overcomes the current limitations of present factor replacement therapies. Progress on this front has led to multiple manuscripts (39 manuscripts since last promotion) and book chapters, national and international State of the Art lectures, extramural funding from the National Institutes of Health, two patents (one additional pending) and pharmaceutical collaborations. The most advanced effort thus far has demonstrated the ability to express bioengineered recombinant factor VIII in the mammary gland such that it can be purified in high yield from the milk of transgenic ruminant animals. The proof of principle was recently published (*J Thromb Hemost*, 2011, *in press*) and transgenic pigs have been generated through a collaboration with the University of Nebraska. This work will facilitate a new application for a Small Business Research grant from the NIH. In recognition of Dr. Pipe's research contributions to the University of Michigan, he was installed as the first Laurence A. Boxer Research Professor of Pediatrics and Communicable Diseases in January of 2011. As a reflection of his national and international recognition, Dr. Pipe has become an ad hoc grant reviewer for the NIH, NHLBI, Canadian Institute for Health Research, French National Research Agency, Technology Foundation STW of Netherlands, Singapore Ministry of Health and the Clinical Research Program for Peking University, China. He is also a reviewer for a number of hematology and general biology journals.

Recent and Significant Publications:

Lu J, Pipe SW, Miao HZ, Jacquemin M and Gilbert GE: A membrane-interactive surface on the factor VIII C1 domain cooperates with C2 domain epitopes for membrane binding and cofactor function. *Blood* 117:3181-3189, 2011.

Ogata K, Selvaraj S, Miao HZ and Pipe SW: Most Factor VIII B domain missense mutations are unlikely to be causative mutations for severe hemophilia A: Implications for genotyping. *J Thromb Hemost* 9:1183-1190, 2011.

Malhotra JD, Miao, H, Zhang K, Pennathur S, Pipe S, Kaufman R: Antioxidants reduce endoplasmic reticulum stress and improve protein secretion. *PNAS* 105:18525-18530, 2008.

Shi J, Pipe SW, Miao HZ, Rasmussen JT, Heegaard CW, Gilbert GE: Lactadherin blocks thrombosis and hemostasis in vivo: correlation with platelet phosphatidylserine exposure. *J Thromb Hemost* 6:1167-1174, 2008.

Pipe SW: The promise and challenges of bioengineered recombinant clotting factors. *J Thromb Hemost* 3:1692-1670, 2005.

Service: Dr. Pipe attends clinic one day a week and he attends on the pediatric hematology/oncology service four weeks per year. He has served as the director of the Special Coagulation Laboratory, providing personalized clinical laboratory consultation for the entire UMHS system and its MLabs affiliates. He has also fostered an academic environment in this

setting leading to peer-reviewed research, expanded laboratory offerings, novel assay development, enhanced laboratory efficiencies and cost-savings for the health system. Since 2008, he has served as division director of pediatric hematology and oncology. In this role he has successfully recruited faculty to expand clinical and research efforts including the first Russell G. Adderley Professorship in Sarcoma Research (Elizabeth Lawlor M.D., Ph.D.), and a Biological Sciences Scholar (Jordan Shavit M.D., Ph.D.). Under his leadership the division has been a departmental leader in the development of clinical practice guidelines. He has been a member of multiple UMHS committees including a term of service on the Institutional Review Board, the Venous Thromboembolism Prevention Committee for the Office of Clinical Affairs tracking and characterizing this important complication in Mott Children's Hospital and devising appropriate screening and prophylaxis strategies, and the Anticoagulation Subcommittee of the Pharmacy and Therapeutics Committee that is drafting policies and guidelines for the entire health system. Nationally he serves on the Medical and Scientific Advisory Committee for the National Hemophilia Foundation, is the Hematology and Oncology Subspecialty chair for the Central Society for Clinical Research, is on the board of directors for the Hemostasis and Thrombosis Research Society and was recently appointed to the Blood Products Advisory Committee to the Centers for Biologics Evaluation and Research at the FDA.

External Reviewers:

Reviewer A: "Dr. Pipe is the consummate physician scientist. He has excelled in his research area of Factor VIII structure and function, measurably adding to the international body of literature focused on the mechanisms behind Factor VIII tracking and cellular expression. Accordingly, he is one of the top five physician scientists in Factor VIII structure and function in the country."

Reviewer B: "Dr. Pipe is an accomplished educator....The Pediatric Hematology/Oncology Program at the University of Michigan has a deservedly high reputation for excellence in clinical care, education and research and Dr. Pipe deserves credit for his role in this sustained achievement."

Reviewer C: "...I think Dr. Pipe is one of the very best physician-scientists interested in coagulation research. Having had the opportunity to review research proposals and scientific credentials of several physician-scientists in the USA, I think Dr. Pipe stands at the top."

Reviewer D: "Over the past several years, Dr. Pipe has garnered a national and international respect for his research in molecular modifications of factor VIII and consequent rational design of novel molecules with important therapeutic implications....Steve is very generous in his educational and presentation contributions to our professional societies where he serves as a mentor and model to junior faculty in hemostasis nationally."

Reviewer E: "He is a maverick for new approaches to hemophilia therapy, while maintaining a very level-headed approach to patient care and clinical issues."

Summary of Recommendation:

Dr. Pipe is an extremely accomplished scientist, clinician and educator who is recognized and respected at national and international levels. I strongly recommend Steven W. Pipe, M.D. for promotion to professor of pediatrics and communicable diseases, with tenure, Department of Pediatrics and Communicable Diseases, and professor of pathology, without tenure, Department of Pathology, Medical School.

A handwritten signature in black ink, appearing to read "J.O. Woolliscroft", written over a horizontal line.

James O. Woolliscroft M.D.

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Lyle C. Roll Professor of Medicine

May 2012