

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF PHARMACOLOGY
DEPARTMENT OF INTERNAL MEDICINE
DEPARTMENT OF SURGERY

Michael A. Holinstat, Ph.D., associate professor of pharmacology, with tenure, Department of Pharmacology, associate professor of internal medicine, without tenure, Department of Internal Medicine, and associate professor of surgery, without tenure, Department of Surgery, Medical School, is recommended for promotion to professor of pharmacology, with tenure, Department of Pharmacology, professor of internal medicine, without tenure, Department of Internal Medicine, and professor of surgery, without tenure, Department of Surgery, Medical School.

Academic Degrees:

Ph.D.	2004	University of Illinois at Chicago
M.S.	2000	University of Illinois at Chicago
B.S.	1995	Southern Connecticut State University

Professional Record:

2017 - Present	Associate Professor of Surgery, University of Michigan
2015 - Present	Associate Professor of Pharmacology (with tenure), University of Michigan
2015 - Present	Associate Professor of Internal Medicine, University of Michigan
2013 - 2015	Associate Professor of Medicine, Thomas Jefferson University
2013 - 2015	Associate Professor of Biochemistry and Molecular Biology, Thomas Jefferson University
2008 - 2013	Assistant Professor of Medicine, Thomas Jefferson University
2008 - 2013	Assistant Professor of Biochemistry and Molecular Biology, Thomas Jefferson University

Summary of Evaluation:

Teaching: Dr. Holinstat has made significant contributions to the department's teaching mission in the areas of cardiovascular pharmacology, platelet signaling, and translational research. Dr. Holinstat has lectured on a diverse and wide range of subjects including, but not limited to antiarrhythmic drugs, autonomic drugs, drugs for treating heart failure, neuromuscular and ganglionic blocking drugs, calcium channel blockers, and antihypertensives, as well as teaching in the areas of signal transduction in cells, receptors, second messengers, and platelet signaling. Institutionally, Dr. Holinstat has participated in and taught several different courses for several departments and colleges at the University of Michigan including, Introduction to Translational Science (Pharm640), Pharmacy 730, Physician Scientist Clinical and Translational Research (MEDADM8447), Mentored Research Practicum (INTMED605), and Translational Pharmacology I (PHARM621). He directed and developed courses as part of the MS in Clinical Research (MSCR) program, and is the director of the TL1 training grant in clinical translational research. He has mentored medical students, graduate students, undergraduate students, post-doctoral fellows, advanced post-graduate fellows, and faculty members, as well as hosted several visiting scholars. His teaching has consisted of classroom instruction, research instruction in the laboratory, participation in graduate student dissertation committee meetings and graduate student seminars, and instruction in the use of platelet studies and analysis. He has also served as a coach for the "R01 Boot Camp" and has participated in the MICHR mentoring academy.

Research: Dr. Holinstat has made many significant contributions to the field cardiovascular disease and platelet activation. His research program focuses on understanding platelet biology spanning from basic science to drug discovery to clinical trials, including a clinical trial focused on platelet function in Type 2 Diabetes Mellitus. His current studies include: identifying inherent racial differences in platelet function by investigating underlying genetic differences in Black and Caucasian populations that predispose some patients to a higher risk for thrombosis and stroke while sparing others; understanding how platelet activation is regulated by the enzyme 12-lipoxygenase (12-LOX); and identifying, screening, and patenting several first-in-human inhibitors highly selective for 12-lipoxygenase. His ongoing work uses animal and human models to translate basic research findings into novel approaches for the regulation of platelet function and limiting thrombosis in vivo in high-risk populations.

Dr. Holinstat is an outstanding scientist who has established an international reputation as an expert in cardiovascular and lipid biology. He is highly sought out as a scientific collaborator and has an extensive list of national and international speaking invitations, including at top meetings in his field. He is highly productive, with 92 peer-reviewed publications in high-quality, peer-reviewed journals such as *Frontiers in Pharmacology*, *Chest*, and the *Journal of Thrombosis and Haemostasis*. He currently serves as the principal investigator on three large industry grants, two from Cereno Scientific and one from Lexicon Pharmaceuticals, as well as the principal investigator on six National Institutes of Health grants (R13, R21, an R01, and three R35 grants). He is also a co-investigator on two other R01s and an American Heart Association grant. His work has resulted in eight patents and five disclosures.

Recent and Significant Publications:

- Yamaguchi, A, Stanger L, Freedman JC, Prieur A, Thav R, Tena J, Holman TR, Holinstat M, “Supplementation with omega-3 or omega-6 fatty acids attenuates platelet reactivity in postmenopausal women,” *Clin Transl Sci*: 2022: PM35791734.
- Yamaguchi A, Stanger L, Freedman CJ, Standley M, Hoang T, Adili R, Tsai WC, van Hoorebeke C, Holman TR, Holinstat M, “DHA 12-LOX-derived oxylipins regulate platelet activation and thrombus formation through a PKA-dependent signaling pathway,” *J Thromb Haemost* 19(3): 839-851, 2021. PM33222370/PMC7925359.
- Tourdot BE, Stoveken H, Trumbo D, Yeung J, Kanthi Y, Edelstein LC, Bray PF, Tall GG, Holinstat M, “Genetic Variant in Human PAR (Protease-Activated Receptor) 4 Enhances Thrombus Formation Resulting in Resistance to Antiplatelet Therapeutics,” *Arterioscler Thromb Vasc Biol* 38(7): 1632-1643, 2018. PM29748334/PMC6023764.
- Adili R, Tourdot BE, Mast K, Yeung J, Freedman JC, Green A, Luci DK, Jadhav A, Simeonov A, Maloney DJ, Holman TR, Holinstat M, “First Selective 12-LOX Inhibitor, ML355, Impairs Thrombus Formation and Vessel Occlusion In Vivo With Minimal Effects on Hemostasis,” *Arterioscler Thromb Vasc Biol* 37(10): 1828-1839, 2017. PM28775075/PMC5620123.
- Tourdot BE, Adili R, Isingizwe ZR, Ebrahim M, Freedman JC, Holman TR, Holinstat M, “12-HETrE inhibits platelet reactivity and thrombosis in part through the prostacyclin receptor,” *Blood Adv* 1(15): 1124-1131, 2017. PM29296755/PMC5728320.

Service: Dr. Holinstat has been an active participant on several institutional and departmental committees at the University of Michigan. He has taken on leadership roles in national societies, including the American Society for Pharmacology and Experimental Therapeutics (ASPET), the Mid-Atlantic Pharmacology Society (MAPS), the International Society for Thrombosis and Hemostasis, and the Association for Clinical and Translational Science. He has served on foundation, federal, and international review committees including the American Heart Association,

ASPET, and the National Institutes of Health. He has served as an ad hoc reviewer for many top-tier scientific journals, as an associate editor for *Frontiers in Integrative and Regenerative Pharmacology*, on the Editorial Review Board for the *Journal of Pediatric Biochemistry*, and as an Editorial Board Member for the *Arteriosclerosis, Thrombosis, and Vascular Biology Journal* and the *Journal of Thrombosis and Hemostasis*. He has organized and chaired symposia at scientific conferences and has served on numerous departmental and institutional committees within the Cardiovascular Center, the Medical School, and Pharmacology.

External Reviewers:

Reviewer A: “He is a national and international leader in platelet physiology and pharmacology whose research contributions are shaping current thinking in the field and may lay the groundwork for uncovering novel approaches to anti-thrombotic therapy. In addition to being an outstanding scientist, he is a team player who is highly collaborative and well respected in the hemostasis and thrombosis community.”

Reviewer B: “Importantly, he has developed an impressive infrastructure for clinical studies and, indeed, was appointed as Director of the TL1 MS program in clinical research...Dr. Holinstat has received significant notoriety within the platelet community...He has an impressive record of grant funding, being PI on an R35, an R21 and on large sponsored research agreements. He is also Director of the Platelet Physiology and Pharmacology Core. He is a valued collaborator and is a co-investigator on several additional grants. He has had several patents issued and several others are pending.”

Reviewer C: “Dr. Holinstat has contributed significantly to his institutions and to national organizations by training students and postdocs, reviewing manuscripts and serving on editorial boards. He has also served on numerous committees, such as grant review committees for the American Heart Association and the National Institutes of Health.”

Reviewer D: “He has chaired several national and regional committees, both focused around science policy as well as scientific leadership. He has dedicated a substantial degree of time and effort to serving the community through abstract and conference and paper and grant review. He has substantially contributed to the field as a speaker and lecturer. I have had the privilege of attending his seminars and lectures and have always been impressed.”

Reviewer E: “Dr. Holinstat has a track record of sustained excellence in discoveries, impactful scholarship, productive research, and key contributions to the research, teaching, and service missions at the local, national, and international scale...His body of published work has been cited more than 4,200 times and...has a h-index of 38: further evidence of the quantity and quality of his academic work, and its reputation and impact in the field...He has also received a number of honors and awards for his scientific discoveries, including the 2012 Kenneth M. Brinkhous Prize in Thrombosis (awarded to one investigator annually), election as a Fellow to the AHA, and selection as an Editorial Board Member to ATVB and JTH.”

Reviewer F: “Dr. Holinstat has had a remarkable track record of sustained high level research support from NIH since establishing his independent lab in Philadelphia in 2008. Currently he is supported by a highly competitive NIH R35 Outstanding Investigator Award, along with an R01 and R21, and he is coinvestigator with David Pinsky on another R01. He also has funding from biotech, showing the translational significance of his research program. Given the highly competitive nature of NIH funding, this clearly shows that the scientific community considers his work to be highly significant and rigorous. Demonstrating his commitment to the next generation of clinical and

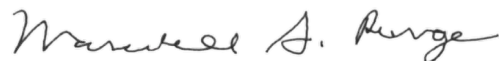
translational scientists, he is the PI for the University of Michigan CTSI-funded TL1 training grant. His record of funding and scientific productivity places Dr. Holinstat in the top 10% of platelet researchers in this country.”

Reviewer G: “Of his recent work, the most impactful has been work to elucidate how polyunsaturated fatty acids (omega 6 docosapentaenoic acid and the active oxylinpin metabolites) may elicit its beneficial CV effects through inhibition of platelet function via peroxisome proliferator activator receptor- α . He has also published important work understanding genetic differences that regulate thrombin signaling in platelets. He has been an invited speaker at numerous venues, including the American Heart Association (AHA) Scientific Sessions and meetings and lectures around the US and world.”

Reviewer H: “Dr. Holinstat is highly regarded scientist, and his work is interesting and clinically significant. He is [sic] world class investigator in platelet signaling, thrombosis and hemostasis...His work is impressive and publication record is outstanding...I consider Dr. Halinstat’s scientific accomplishment and contribution are on [sic] the top 10 percentile in his peer group...excellent public servant who has served in many study sections of various organization [sic] including NIH. He is the member of several editorial boards such as ATVB and JTH, etc.”

Summary of Recommendations:

Dr. Holinstat is an internationally recognized expert in cardiovascular pharmacology with a focus on platelet biology and signaling research. He has made significant contributions to the field of hemostasis and thrombosis and our understanding of the basic mechanisms underlying protease-activated receptor biology and lipoxygenase pharmacology. He has emerged as a leader in these research areas and is recognized for his deep expertise in biochemistry, molecular biology, pharmacology, and physiology. He is held in high esteem by his colleagues and peers. He has demonstrated a significant commitment to teaching, making valuable contributions to the teaching, and mentoring of graduate students and post-doctoral fellows in the laboratory, as well as to graduate students and medical students in the classroom. His service to national organizations is outstanding and his accomplishments in his field to date are reflected by the numerous national and international awards he has received. Therefore, I am pleased to recommend Michael A. Holinstat, Ph.D. for promotion to professor of pharmacology, with tenure, Department of Pharmacology, professor of internal medicine, without tenure, Department of Internal Medicine, and professor of surgery, without tenure, Department of Surgery, Medical School.



Marschall S. Runge, M.D., Ph.D.
Executive Vice President for Medical Affairs
Dean, Medical School

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