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

<u>Goutham Narla, M.D., Ph.D.</u>, associate professor of internal medicine, with tenure, Department of Internal Medicine, Medical School, is recommended for promotion to professor of internal medicine, with tenure, Department of Internal Medicine, Medical School.

Academic Degrees:

M.D.	2006	Mt. Sinai School of Medicine
Ph.D.	2006	Mt. Sinai School of Medicine
B.S.	1997	Santa Clara University, California

Professional Record:

2018-preseent	Associate Professor of Internal Medicine, University of Michigan
2016-2018	Associate Professor of Medicine, Case Western Reserve University
2012-2016	Assistant Professor of Medicine, Case Western Reserve University
2010-2012	Assistant Professor of Medical Education, Mount Sinai University
2009-2012	Assistant Professor of Genetics and Genomic Sciences and Medicine,
	Mount Sinai University
2008	Instructor of Genetics and Genomic Sciences and Medicine,
	Mount Sinai University

Summary of Evaluation:

<u>Teaching</u>: Dr. Narla serves as the medical scientist training program associate director, where he provides mentorship and career guidance to undergraduate and graduate students, fellows and faculty in formal and informal gatherings. He provides a weekly lecture on oncogene and tumor suppressor biology to graduate and medical students and continuing medical education lecturers to providers on identifying high risk cancer genetic families. Dr. Narla's most important teaching contribution is the many invited Grand Rounds presentations at national and international scientific communities on the role of protein phosphatases in cancer and how to develop drugs to therapeutically reactivate these proteins. He has served on 14 thesis committees.

<u>Research</u>: Dr. Narla's research focus is on understanding the mechanisms driving human cancer development and progression. His research has led to the identification of a new class of tumor suppressor genes in human cancer, the characterization of novel mechanisms of tumor suppressor gene inactivation in cancer progression, the development and validation of pharmaceutically tractable strategies to reactive tumor suppressor gene function for the treatment of a broad range of human cancers, and the structural, functional and biological mechanisms of PP2A inactivation in human cancer. He is the principal investigator of two National Institutes of Health R01 grants and has three other NIH and Department of Defense awards highlighting the collaborative and multi-disciplinary nature of his work. Dr. Narla has numerous active collaborations in the field of protein phosphatase 2A structure, biology and

drug development with national and international collaborators tha have resulted in multiple cosenior or co-authored publications including three major ones published in *Science Translational Medicine*, *Cancer Discovery* and *Molecular Cancer Therapeutics* in the last year. He co-leads intra- and inter-departmental research collaborations in the fields of polygenic risk score dissemination to the clinic. Dr. Narla has published more than 80 peer-reviewed articles, and has been invited to present his research on 46 occasions regionally, nationally and internationally.

Recent and Significant Publications:

Sarah E Taylor, Caitlin M O'Connor, Zhizhi Wang, Guobo Shen, Haichi Song, Daniel Leonard, Jaya Sangodkar, Corinne LaVasseur, Stefanie Avril, Steven Waggoner, Kristine Zanotti, Amy J Armstrong, Christa Nagel, Kimberly Resnick, Sareena Singh, Mark W Jackson, Wenqing Xu, Shozeb Haider, Analisa DiFeo and Goutham Narla. The highly recurrent PP2A A α -subunit mutation P179R alters protein structure and impairs PP2A enzyme function to promote endometrial tumorigenesis. *Cancer Research*, August 15;79(15):4242-4257, 2019.

O'Connor, C., Hoffa, M., Taylor, S., Avelar, R., Narla, G. Protein phosphatase 2A Aα regulates Aβ protein expression and stability. *J. Biol. Chem*, Apr 12:294:5923, 2019.

Tohmé R, Izadmehr S, Gandhe S, Tabaro G, Vallabhaneni S, Thomas A, Vasireddi N, Dhawan NS, Ma'ayan A, Sharma N, Galsky MD, Ohlmeyer M, Sangodkar J, Narla G. Direct activation of PP2A for the treatment of tyrosine kinase inhibitor-resistant lung adenocarcinoma. *JCI Insight*. Feb 21;4(4), 2019.

Kauko O, O'Connor CM, Kulesskiy E, Sangodkar J, Aakula A, Izadmehr S, Yetukuri L, Yadav B, Padzik A, Laajala TD, Haapaniemi P, Momeny M, Varila T, Ohlmeyer M, Aittokallio T, Wennerberg K, Narla G, Westermarck J. PP2A inhibition is a druggable MEK inhibitor resistance mechanism in KRAS-mutant lung cancer cells. *Sci Transl Med.* Jul 18;10(450), 2018.

Sangodkar J, Perl A, Tohme R, Kiselar J, Kastrinsky DB, Zaware N, Izadmehr S, Mazhar S, Wiredja DD, O'Connor CM, Hoon D, Dhawan NS, Schlatzer D, Yao S, Leonard D, Borczuk AC, Gokulrangan G, Wang L, Svenson E, Farrington CC, Yuan E, Avelar RA, Stachnik A, Smith B, Gidwani V, Giannini HM, McQuaid D, McClinch K, Wang Z, Levine AC, Sears RC, Chen EY, Duan Q, Datt M, Haider S, Ma'ayan A, DiFeo A, Sharma N, Galsky MD, Brautigan DL, Ioannou YA, Xu W, Chance MR, Ohlmeyer M, Narla G. Activation of tumor suppressor protein PP2A inhibits KRAS-driven tumor growth. *J Clin Invest*. 2017 Jun 1;127(6):2081-2090, 2017.

<u>Service</u>: Dr. Narla is an active member of several professional endeavors. He is a member of the American Association for Cancer Research, American Society for Clinical Investigation, American Society of Hematology and the American Society for Biochemistry and Molecular Biology. He is a scientific reviewer for the Department of Defense and an editorial reviewer for *Oncogene*, *Cancer Research*, and *Proceedings of National Academy of Sciences*. Dr. Narla is a permanent member of the American Cancer Society TBG Study Section, is the president of

the Young Scientist Foundation, and an annual meeting leader of the Howard Hughes Medical Institute. Departmentally, he is a member of the Program Evaluation Committee for the Genetics Residency Program.

External Reviewers:

<u>Reviewer A</u>: "...as a [junior] independent investigator, Dr. Narla has continued to be extraordinarily productive with many peer-reviewed papers, including papers in *Science* and *Nature Genetics*. His research has also been supported by an Early Career Award from the Howard Hughes Medical Institute (HHMI), a high honor indeed...Dr. Goutham Narla is an exceptional physician-scientist who has excelled at the very highest levels in both research and clinical medicine. As a result, Dr. Narla serves as a remarkable role model for [junior] faculty and students, as well as for his peers and colleagues. On a personal level, he is an ideal colleague – warm, friendly, and eager to share ideas."

<u>Reviewer B</u>: "He went on to pursue additional mechanistic studies relating to the function and mechanism by which PP2A can regulate oncogenesis using multiple orthogonal models and platforms. This work is very important and may have implications to not only understanding the mechanisms of prostate and lung cancer development and progressions, but also for the ultimate treatment of these diseases, especially in patients who develop tyrosine kinase resistance...In conclusion, I strongly support the promotion of Dr. Goutham Narla to the rank of Professor with Tenure at the University of Michigan (instructional track)."

<u>Reviewer C</u>: "Dr. Narla has an innovative research program that has stimulated considerable excitement in the field and has opened up for new potential therapeutic avenues in cancer... Dr. Narla has established an innovative and productive independent laboratory and is a highly regarded physician and mentor. He has built both a national and international reputation for his work. Although my institution has unusually high metrics for promotion, Dr. Narla has clearly made both substantial and sustained contributions to his fields and has established a productive and well-funded laboratory. His scholarly work is impressive and his service contributions remarkable. He is an outstanding candidate for appointment to Professor at the University of Michigan, and I endorse him with my highest recommendation and without reservation."

<u>Reviewer D</u>: "Since moving to the University of Michigan, Dr. Narla has continued his upward trajectory with 17 additional publications, four of which are included in his highlighted publications. In addition, he has continued his excellent record of grant funding with at least 3 new grant awards and multiple pending grants. There is every indication that he will continue to be productive at a high level and would be an asset to any university."

<u>Reviewer E</u>: "Overall, while this faculty is only than [sic] ten years out of his training and in some respects only a mid-career investigator, his research career got an early jump start as an MD/PhD and then a junior Howard Hughes investigator. Moreover, I am convinced that the promotion is warranted based to a large extent on his recent success in funding. He has made significant and original contributions to science in 2 important fields (KLF6 and PP2A). He has had steady productivity in competitive journals. And he has recently taken on a significant leadership and administrative role (Division Chief in Genetic Medicine)."

Summary of Recommendations:

Dr. Narla has already made significant research contributions in understanding the mechanisms driving human cancer development and progression, and has impacted cancer treatments by opening up new potential therapeutic avenues for cancer patients. I am pleased, therefore, to recommend Goutham Narla, M.D., Ph.D. for promotion to professor of internal medicine, with tenure, Department of Internal Medicine, Medical School.

Marchell A. Renge

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

May 2020