Approved by the Regents
May 17, 2018

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF MICROBIOLOGY AND IMMUNOLGY

Akira Ono, Ph.D., associate professor of microbiology and immunology, with tenure, Department of Microbiology and Immunology, Medical School, is recommended for promotion to professor of microbiology and immunology, with tenure, Department of Microbiology and Immunology, Medical School.

Academic Degrees:

Ph.D.	1994	University of Tokyo
M.S.	1991	University of Tokyo
B.S.	1989	Waseda University, Tokyo

Professional Record:

2012-present	Associate Professor of Microbiology and Immunology, University of Michigan
2005-2012	Assistant Professor of Microbiology and Immunology, University of Michigan

Summary of Evaluation:

Teaching: Dr. Ono is a dedicated and capable teacher of department courses for medical and graduate students. Since his last promotion, he has taught the ID/Micro Small Group sequence (ID/Microbiology 500) for M1 medical students, Pharmacology 502 (grant writing), Microbiology 813 (Science in the Clinics) and PIBS 503 (Research Responsibility and Ethics) for graduate students. In the ID/Micro Small Group sequence, Dr. Ono commits roughly 36-44 hours of contact and presentation time, with additional time devoted periodically to sequence restructuring. For Pharmacology 502, he teaches grant writing. This involves approximately 12 contact hours. For Microbiology 813, he teaches Ph.D. students and research fellows, and he discusses contemporary primary research papers on microbiology that have clinical relevance. Lastly, for PIBS 503, he teaches Research Responsibility and Ethics. This involves one contact hour. He consistently receives strong evaluations from his students. He has also served on dissertation committees for 17 graduate students in the Department and around the Medical School. Finally, Dr. Ono is a highly skilled mentor for post-doctoral fellows and graduate students in his laboratory. He expertly guides his trainees to develop their scientific knowledge and skills and prepares them for professional careers in science.

Research: Dr. Ono has made significant contributions in the field of retrovirus biology and pathogenesis. Since his last promotion in 2012, he has unequivocally established himself as an expert and leader in HIV-1 Gag-membrane interactions. He and his group have demonstrated that RNA binding to the MA domain of the Gag protein modulates the lipid binding activity of Gag

and controls the locations within infected cells that HIV is assembled. Furthermore, he has discovered that RNA interaction with MA domains is a general paradigm that regulates membrane targeting and assembly of retroviruses other than HIV. Another major discovery of Dr. Ono's is that HIV assembles primarily within the uropod of infected T cells. He has established some of the key molecular mechanisms involved and has demonstrated that uropod assembly is critical for subsequent HIV transmission. In addition to his independent research, Dr. Ono has also been instrumental in several collaborative projects. With David Markovitz in the Department of Internal Medicine, Dr. Ono is studying the human endogenous retrovirus K (HERVK). This work is funded by an NIH transformative R01 award. Dr. Ono is also working collaboratively with Dr. Karin Musier-Forsythe at The Ohio State University on an R01 for which he is a co-investigator with effort. The impact and influence of Dr. Ono's work are also evidenced by the awarding of an R37 MERIT award from the NIH. These grants are awarded to investigators who submit highly scored NIH R01 applications, and they enable up to 10 years of funding. They are intended to "provide long-term grant support to investigators whose research competence and productivity are distinctly superior and who are highly likely to continue to perform in an outstanding manner." His work is highly regarded, having been cited 3,409 times, with an h-index of 27. Additionally, his widely appreciated expertise has led to invitations to chair sessions or to speak at important meetings in the field of retrovirology, as well as to write review articles covering recent literature in the field of virus assembly mechanisms.

Recent and Significant Publications:

Chukkapalli V, Inlora J, Todd GC, Ono A: Evidence in support of RNA-mediated inhibition of phosphatidylserine-dependent HIV-1 Gag membrane binding in cells. *Virol* 87:7155-7159, 2013.

Inlora J, Collins DR, Trubin ME, Chung JY, Ono A: Membrane binding and subcellular localization of retroviral Gag proteins are differentially regulated by MA interactions with phosphatidylinositol-(4,5)-bisphosphate and RNA. *MBio* 5:e02202, 2014.

Olety B, Veatch SL, Ono A: $PI(4,5)P_2$ acyl chains differentiate membrane binding of HIV-1 Gag from that of the phospholipase Cδ1 PH domain. *J Virol* 89:7861-7873, 2015.

Grover JR, Veatch SL,* Ono A*: Basic motifs target PSGL-1, CD43, and CD44 to plasma membrane sites where HIV-1 assembles. *J Virol* 89:454-467, 2015. (* co-corresponding authors)

Todd GC, Duchon AA, Inlora J, Olson ED, Musier-Forsyth K, Ono A: Inhibition of HIV-1 Gag-membrane interactions by specific RNAs. *RNA* 23:395-405, 2017.

Service: Dr. Ono serves ably on faculty committees, bringing the same focus and insight to these activities as he does to his research and teaching. In the Department of Microbiology and Immunology, he has served on the Graduate Studies Committee, Departmental Appointments, Promotions and Awards Committee, on the Faculty Search Committee for Cluster Hiring (Multi-scale Cell Mechanics hire), he has organized the department's research retreat, and he now serves as the chair of the department's active Diversity, Equity and Inclusion Committee. At the institutional level, Dr. Ono served on admissions committees, advisory committees, the Committee on Student Biomedical Research Programs, the Genetics Training Program Executive Committee,

the Cell and Molecular Biology Program Selection Committee, the Institutional Biosafety Committee and finally, he has served as a faculty ally for diversity in graduate education for the Rackham Graduate School at UM. At the national and international levels, he served as a reviewer for several high-profile journals and as a guest editor or editorial board member for numerous other journals. He reviewed grant applications for several international research funding agencies and has served as session co-chair, session chair, convener, and discussant for several national and international meetings. Thus, Dr. Ono's efforts are contributing in key ways to the future excellence of our mission.

External Reviewers:

Reviewer A: "Since 2010, Dr. Ono's lab has continued advancing the field of HIV-1 assembly with a number of first rate investigations. These have been reported in three exceptional papers in 2013, three exceptional papers in 2015, an imaginative set of experiments using giant unilamellar vesicles, a collaborative investigation with the Musier-Forsyth lab, and a collaborative report on how the tumor suppressor APC promotes HIV-1 assembly."

Reviewer B: "Dr. Ono's contributions in the past and currently continue to provide very important insights into aspects of retrovirus assembly particularly with regard to Gag=membrane interactions....He was on a clear trajectory when he became an Associate Professor. Since that time, he has unequivocally established himself as an expert and leader in HIV-1 Gag-membrane interactions whose work is globally recognized."

Reviewer C: "Dr. Ono is an internationally recognized virologist with specific expertise in the assembly of retroviruses. He is a standout leader in this field who has made seminal contributions to the understanding of how the viral Gag protein of retroviruses such as HIV-1, which drives viral assembly, interacts with specific host cell membrane molecules – both proteins and lipids – during viral assembly."

Reviewer D: "Dr. Ono is extremely highly regarded in the field of retrovirus molecular biology, assembly, and RNA packaging for many reasons, including the very high quality and impact of his publications; the creative approaches and groundbreaking directions he has taken; his collegiality in terms of discussing his data, sharing reagents, and being fair and thoughtful in his assessment of other work in the field; and his willingness to dialogue with other researchers openly and enthusiastically."

Reviewer E: "The quality of Dr. Ono's research is exceptionally high and his research group standardly publishes outstanding papers. We routinely cite Dr. Ono's publications in our own work given that we recognized them as being highly significant in advancing knowledge in the general field of retroviral assembly....He is respected both as an intellectual and for his oversight of a research program that regularly makes meaningful contributions to the field that have contributed new knowledge that continues to advance our understanding of the mechanisms of HIV particle assembly and release from infected cells."

Reviewer F: "Briefly stated, Akira's work is always outstanding and always significant. It is evident from his CV that he is also a conscientious member of the research community, contributing to reviews of many manuscripts and serving on study sections."

Reviewer G: "Akira is widely (and correctly!) viewed as a leader in HIV molecular virology...and his thorough and methodical approach can belie his passion and keen intellect…I would personally rank him as one of the international leaders in the field of HIV assembly."

Summary of Recommendation:

Dr. Ono has distinguished himself as an outstanding researcher who has earned the respect of his peers in the field and the admiration of his Michigan colleagues. He is a leader in a highly competitive and important field of research. He has made outstanding contributions in research, teaching and service, and he shows great promise for continued growth as a scholar and colleague. I enthusiastically recommend Akira Ono, Ph.D. for promotion to professor of microbiology and immunology, with tenure, Department of Microbiology and Immunology, Medical School.

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

May 2018