Approved by the Regents
May 15, 2014

PROMOTION RECOMMENDATION
The University of Michigan
School of Dentistry

Yuji Mishina, PhD, associate professor of dentistry, without tenure, School of Dentistry, is recommended for promotion to professor of dentistry, with tenure, School of Dentistry.

Academic Degrees:

Ph.D.	1986	University of Tokyo, Tokyo, Japan, Molecular Biology
M.S.	1983	University of Tokyo, Tokyo, Japan, Molecular Biology
B.S.	1981	University of Tokyo, Tokyo, Japan, Biology

Professional Record:

2008-Present	Associate Professor, without tenure, Department of Biologic and Materials Sciences, School of Dentistry, University of Michigan, Ann Arbor, MI
1998-2008	Group Head, Molecular Developmental Biology Group, Laboratory of Reproductive and Developmental Toxicology, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC
1992-1998	Post-doctoral Fellow, M.D. Anderson Cancer Center, The University of Texas, TX
1986-1992	Research Associate, Kihara Institute for Biological Research, Yokohama City, University, Yokohama, Japan

Teaching:

Professor Mishina is an excellent and enthusiastic teacher. He contributes to the teaching mission of the school through didactic lectures and mentoring of pre-doctoral and graduate students, research fellows, and junior faculty. He was course director of the Musculoskeletal System segment of the Biomedical Sciences course Dent 538 and the Development and Embryogenesis segment of the Cell and Molecular Biology course Dent 525. He also lectured in the development segment of the Development, Regeneration and Genetics course Dent 539. As a scientist with extensive expertise in developmental biology and an in-depth understanding of human physiology, he is able to easily translate his knowledge to first year dental students. He also participates weekly in Oral Health Science graduate student seminars and organizes monthly craniofacial biology research meetings. As evidenced by his peer and student course evaluations, Professor Mishina is a very conscientious, well-prepared and engaging instructor. However, his real teaching expertise, and where he truly excels, is in training, mentoring and co-mentoring students, research fellows and junior faculty within his laboratory. Since coming to Michigan, he has mentored eight Undergraduate Research Opportunity Program (UROP) students, two Oral Health Science PhD research rotation students, five

post-doctoral fellows and three junior faculty members, as well as several visiting investigators and summer students. His strengths as a research advisor are having a significant influence on many aspiring junior scientists. This is evidenced by the number of former students and mentees who have received grant support through the K99/R00, R01 and R03 award mechanisms. His ability to inspire others and help them achieve their goals brings recognition to his laboratory as well as our institution. This is achieved because of Professor Mishina's hands-on mentoring and dedication to teaching.

Research:

Professor Mishina's research is in the areas of bone biology and cancer. He is focused on understanding how bone morphogenetic proteins (BMPs) regulate embryogenesis and organogenesis. His current work is directed to the study of BMP function in bone formation and remodeling; in cranial neural crest differentiation; and in cilia roles in embryonic left/right asymmetries. His broad discipline is developmental biology in which he is an expert in embryogenesis and development in general and on organogenesis of the skeleton, the heart and gonads. In a new series of objectives he seeks to clarify the molecular pathogenesis of the Ellis-van Cleveld syndrome, which features chondrodysplastic dwarfism and various craniofacial defects. Productivity from the extensive and complex sets of collaborations is quantified by an extensive publication list. Since coming to Michigan in 2008, Professor Mishina has published 46 papers and is senior author on 17 of those. In all, Professor Mishina has published 133 papers. The quantity of his publications is prodigious; they derive from his multiple research collaborations as well as substantial first and senior author contributions. They appear in highly regarded journals such as *Development, Nature Medicine*, the *Proceedings of the National Academy of Sciences*, and *the Journal of Biological Chemistry*.

Professor Mishina has been very successful in obtaining funding that includes a recent NIH R01 grant to support the BMP studies. He is also a co-investigator with major subcontracts on three other R01 grants, as well as a major grant from the Department of Defense in collaboration with an investigator from Carnegie Mellon University. Several new large grant proposals have also been submitted. This is an outstanding achievement given the current funding environment and clearly attests to his ability to innovate and translate his findings into compelling science. In addition to his demonstrated success in peer review, Professor Mishina has added 31 invited lectures and seminars to his list of presentations, for a total of 123 in his career, indicating an impressive national and international reputation. Professor Mishina's academic career is characterized by an unusually high degree of collaboration. A prediction of future success can be made with the highest confidence.

Recent and Significant Publications:

Kamiya, N., Ye, L., Kobayashi, T., Lucas, D. J., Mochida, Y., Yamauchi, M., Kronenburg, H., Feng, J. Q., and Mishina, Y. Disruption of BMP Signaling in osteoblasts through type IA receptor (BMPRIA) increases bone mass. *J. Bone Miner. Res.* 23:2007-2017, 2008.

Yu, P. B., Deng, D. Y., Lai, C. S., Hong, C. C., Cuny, G. D., Bouxsein, M. L., Hong, D. W., McManus, P. M., Katagiri, T., Sachidanandan, C. S., Kamiya, N., Fukuda, T., Mishina, Y., Peterson, R. T., and Bloch, K. D. BMP type I receptor inhibition prevents ectopic ossification in a mouse model of fibrodysplasia ossificans progressiva. *Nat. Med.* 14:1363-1369, 2008.

Kamiya, N., Ye, L., Kobayashi, T., Mochida, Y., Yamauchi, M., Kronenburg, H., Feng, J. Q., and Mishina, Y. BMP signaling in osteoblasts reduces bone mass by negatively regulating Wnt canonical signaling through sclerostin. *Development.* 135:3801-3811, 2008.

Nomura-Kitabayashi, A., Phoon, C. K. L., Kishigami, S., Rosenthal, J., Yamauchi, Y., Abe, K., Yamamura, K., Samtani, R., Lo, C., and Mishina, Y. Outflow tract cushions perform a critical valve-like function in the early embryonic heart requiring BMPRIA-mediated signaling in cardiac neural crest. *Am. J. Physiol. Heart Circ. Physiol.* 297:H1617-1628, 2009.

Kamiya, N., Kobayashi, T., Mochida, Y., Yu, P.B., Yamauchi, M., Kronenberg, H.M., and Mishina, Y. Wnt inhibitors Dkk1 and Sost are downstream targets of BMP signaling through the type IA receptor (BMPRIA) in osteoblasts. *J. Bone Miner. Res.* 25:200-210, 2010.

Miura, S., Singh, A.P., and Mishina, Y. Bmpr1a is required for proper migration of the AVE through regulation of Dkk1 expression in the pre-streak mouse embryo. *Dev. Biol.* 341:246-254, 2010.

Komatsu, Y., Kaaritnen, V., and Mishina, Y.: Cell cycle arrest in node cells governs ciliogenesis at the node to break left-right symmetry. *Development.* 138:3915-3920, 2011.

Kamiya, N., Kaartinen, V. M., and Mishina, Y. Loss-of-function of ACVR1 in osteoblasts increases bone mass and activates canonical Wnt signaling through suppression of Wnt inhibitors SOST and DKK1. *Biochem. Biophys. Res. Comm.* 414:326-330, 2011.

Wang, S.-K., Komatsu, Y., and Mishina, Y. Potential contribution of neural crest cells to dental enamel formation. *Biochem. Biophys. Res. Comm.* 415:114-119, 2011.

Liu, H.X., Komatsu, Y., Mishina, Y., and Mistretta, C.M.: Neural crest contribution to lingual mesenchyme, epithelium and developing taste papillae and taste buds. *Dev. Biol.* 368:294-303, 2012.

Komatsu, Y., Yu, P.B., Kamiya, N., Pan, H., Fukuda, T., Scott, G.J., Ray, M.K., Yamamura, K., and Mishina, Y. Augmentation of Smad-dependent BMP signaling in neural crest cells causes craniosynostosis in mice. *J. Bone Miner. Res.,* accepted on Dec. 5, 2012.

Schulz, T. J., Huamg, P., Huang, T.L., McDougall, E., Townsend, K.L., Cypess, A.M., Mishina, Y., Gussoni, E., Tsung, Y.H. Brown fat paucity due to impaired BMP signaling induces compensatory browning of white fat. *Nature,* 495, 379-383, 2013.

Service:

Professor Mishina has made great strides in service in the last two years. He has increased his involvement substantially both in the School of Dentistry and at the university level. He has served on five dental school committees; the Grievance Panel, Vision Team Committee for Biomedical Sciences Core, Oral Health Sciences Seminar Committee (chair), Research Committee, Preliminary

Examination Committee of the Oral Health Sciences PhD Program. He also organized a series of meetings to review grant applications for the school that has been very beneficial to many investigators. At the university level, he has served on the Biomedical Research Council Bridging Support Program and the Extended Research Bridging Program. At present he serves on the University Committee on Use and Care of Animals (UCUCA) that is an onerous and extremely important task that few faculty accept due to the substantial time commitment. He should be commended for his dedication to animal health and well-being. Nationally he is on the editorial board for seven journals including the *Journal of Bone and Mineral Research*, the flagship journal for the American Society for Bone and Mineral Research, and the *Journal of Dental Research*. He participates as an ad hoc reviewer for several grant programs and manuscript reviews. His list as an invited speaker continues to grow, as does the importance of the meetings he attends and the presentations he delivers. He is actively submitting, presenting and publishing abstracts nationally and internationally.

External Reviewers:

Reviewer (A): "In addition to his publications in leading journals, Yuji's structure in his field of research is exemplified by being an invited lecturer at many institutions both in the United States and abroad. It is amazing that he has given 125 invited presentations at prestigious institutions. His stature as a leader in his field is further confirmed by his services on various grant review panels and by his peer review and editorial board activities for several biomedical journals."

Reviewer (B): "Dr. Mishina's studies have also led to key new insights into craniosynostosis, wherein the cranial sutures fuse prematurely, a frequent syndrome in humans."

Reviewer (C): "In our field and also in the broader area of developmental biology, his peers regard Dr. Yuji Mishina as one of the excellent world leaders."

Reviewer (D): "He continues to make significant contributions through the development of novel regents and mouse models of BMP signaling that he generously distributes to scientists throughout the world."

Reviewer (E): "He has created many mouse models to study the function of BMP in skeletal, craniofacial, heart, ciliogenesis and its subsequent role in left-right symmetry and chondrogenesis. He has used mice with mutation in BMPs or its several receptors for this purpose. I have no doubt that these lines of work are unique and will provide him with significant and high impact papers in the future as well as attract grant funding at the same time."

Summary of Recommendation:

Professor Mishina has established himself as an outstanding and much sought after developmental biologist and geneticist who has made several important advances in our understanding of BMP action in bone development and regeneration. He secured strong extramural support for his laboratory and is a prolific author and collaborative scientist. His commitments to teaching and service have been of uniform high quality. The consistency and strength of his contributions permit a confident prediction of future success. With the support of the School of Dentistry's Executive Committee, I am pleased to recommend Yuji Mishina, PhD for promotion to professor, with tenure, School of Dentistry.

Laurie K. McCauley, DDS, MS, PhD
Dean, School of Dentistry

May 2014