PROMOTION RECOMMENDATION
The University of Michigan
School of Dentistry

Noriaki Ono, assistant professor of dentistry, School of Dentistry, is recommended for promotion to associate professor of dentistry, with tenure, School of Dentistry.

Academic Degrees:

PhD	2007	Philosophy, Tokyo Medical and Dental University
DDS	2003	Tokyo Medical and Dental University, School of Dentistry

Professional Record:

2014 – Present	Assistant Professor of Dentistry, Department of Orthodontics and Pediatric Dentistry, School of Dentistry, University of Michigan
2012 – 2014	Instructor, Endocrine Unit, Massachusetts General Hospital and Harvard Medical School

Summary of Evaluation:

Teaching: Professor Ono provides vital teaching in the pre-doctoral, graduate and PhD programs at the School of Dentistry. Currently, he is the course director of three graduate didactic courses and an instructor in three other graduate and PhD didactic courses. Additionally, he contributes a considerable effort teaching in the pediatric dentistry orthodontic clinic and the pre-doctoral orthodontic clinic. His teaching evaluations have been consistently high both in didactic and clinical teaching. The students praise him for being knowledgeable, patient, helpful, and giving good advice on clinical procedures. His peers praise him for his presentation style, commitment to teaching, and supportive outlook to all students. His philosophy describes a thoughtful approach to teaching that considers the importance of independent learning, respect, role modeling, and clinical thinking.

Professor Ono is a highly active research mentor. He has been the primary mentor of three MS student research projects in orthodontics and has been on six additional Master's Thesis committees. He mentored six PhD student projects, one DDS student, two undergraduate students, and six post-doctoral fellows of which he was the primary mentor to four. His post-doctoral fellows have been fully independent with numerous publications supporting Professor Ono's commitment to research training. Additionally, he is currently participating as a mentor in the faculty launch program of a new junior investigator on campus.

Professor Ono has shown significant involvement in teaching at the School of Dentistry and has taken advantage of his unique position to teach basic and clinical sciences simultaneously thus, increasing the significance and relevance of the information being delivered. His critical thinking-centered teaching strategies and his delivery are well received by students and peers demonstrating the quality of his teaching. This along with his high level of mentoring activities displays his leadership as an educator shaping the future leaders of dentistry.

Research: Professor Ono's research focuses on the fundamental characteristics of skeletal stem cells that play important roles in bone growth, maintenance, and repair, with the ultimate goal of having an impact on bone regeneration. In rank, he has 21 peer-reviewed publications (first or senior author on 10) in high impact journals such as *Nature Cell Biology*, *Cell Stem Cell*, *Journal of Clinical Investigation*, and *PNAS*. Additionally, he has six book chapters and 41 abstracts. He has been invited to speak at 13 national and international professional meetings such as the 9th International

Orthodontic Congress, American Society for Bone and Mineral Research Annual Meetings, and European Calcified Tissue Society Annual Congress. Additionally, he has been invited to present at eight conferences at other institutes and universities and four at the University of Michigan. He has developed collaborations within the School of Dentistry, the Center of Organogenesis, and the Michigan Integrative Musculoskeletal Health Core Center. His scientific endeavors concentrate on PTH signaling and its impact on chondrocyte and osteoblast lineages. This work was initiated in his K99/R00-supported investigations which were subsequently expanded into an R01 that was awarded in 2018. Currently, he is a co-PI on one University of Michigan MCubed award, is a co-I on another NIH funded project, and has three NIH grants submitted as the PI.

Professor Ono is a creative and ambitious investigator who is committed to excellence. He is a generous colleague, willing to offer his assistance in solving experimental challenges to others and many students whom he mentors. He is recognized as a junior, rising leader in the field of skeletal cell lineage analyses as evidenced by his many invited lecturers and book chapters. Impressively, his H-index is 16 and he has more than one-thousand citations.

Recent and Significant Publications:

Ono N, Ono W, Nagasawa T. Kronenberg HM. 2014. A subset of chondrogenic cells provides early mesenchymal progenitors in growing bones. *Nat Cell Biol.* 16(12):1157-67. IF=19.7

Ono N, Kronenberg HM. 2016. Bone repair and stem cells. *Curr Opin Genet Dev.* 40:103-107. IF=5.8

Sakagami N, Ono W, Ono N. 2017. Diverse contribution of Col2a1-expressing cells to the craniofacial skeletal cell lineages. *Orthod Craniofac Res.* Suppl 1:44-49. IF=2.1

Sakagami N, Matsushita Y, Howle-Syklawer S, Kronenberg HM, Ono W, Ono N. 2018. Msx2 marks spatially-restricted populations of mesenchymal precursors. *J Dent Res.* 97(11):1260-1267. IF=5.4

Mizuhashi K, Ono W, Matsushita Y, Sakagami N, Takahashi A, Saunders TL, Nagasawa T, Kronenberg HM, Ono N. 2018. Resting zone of the growth plate harbors a unique class of skeletal stem cells. *Nature.* 563(7730):254-258. IF=41.6

Takahashi A, Nagata M, Gupta A, Matsushita Y, Yamaguchi T, Mizuhashi K, Maki K, Ruellas AC, Cevidanes LS, Kronenberg HM, Ono N, Ono W. 2018. Autocrine regulation of mesenchymal progenitor cell fates orchestrates tooth eruption. *Proc Natl Acad Sci U S A.* doi: 10.1073/pnas.1810200115. IF=9.5

Mizuhashi K, Nagata M, Matsushita Y, Ono W, Ono N. 2019 Growth plate borderline chondrocytes behave as transient mesenchymal precursor cells. J Bone Mineral Res., 34(8):1387-1392. IF=6.3

Service: Professor Ono's contributions to service supports the school's service mission. From 2016-2019, he served as the co-director of the orthodontic graduate research program. In 2019, he was appointed as the director of the orthodontic graduate research program carrying a high-level of responsibility and student research engagement. Additionally, in the department, he is a member of the Resident Admissions Committee and is an oral comprehensive examiner. At the school level, he has served on the Grievance Hearing Board for the tenure track faculty, Task Force for School of Dentistry Indirect Cost Use, Dentistry Research Committee, Research Day Judge, two tenure-track faculty searches, the faculty search for the associate dean for research, and 12 dissertation committees. At the university level, he serves on the Organogenesis Seminar Series Organizing Committee, and at the national and international level, he is a member of the American Association for Dental Research Edward H. Hatton Awards Committee, and the International Federation of Musculoskeletal Research Societies Scientific Program Committee. He is on the *Journal of Bone and Mineral Research* editorial board and is a manuscript reviewer for numerous journals, such as *PLOS Genetics*, *Nature Communications*, *International Journal for Molecular Sciences*, *JBMR Plus*,

Stem Cells, *Journal of Bone and Mineral Research.* Professor Ono was a grant reviewer for the French National Research Agency, The Generic Call of Proposals, and the American Association of Petroleum Geologists.

External Reviewers:
Reviewer A: "He has clearly established himself as one of the leaders in the field of skeletal stem cells, in particular, the use of mouse developmental genetics to define distinct stem cell populations in long bones, and to lesser extent teeth. His papers stand out by their exceptional quality, and my impression is of a careful and rigorous junior faculty who will continue to establish his reputation in the musculoskeletal field... His recent *Nature* paper is highly influential as it validates a long-standing model that the resting zone of the growth plate harbors stem cells that feed cartilage growth through embryogenesis and post - natal stages. Further, he was able to isolate a particular subset of Pthrp - expressing cells within the resting zone that exhibited stem cell activity. While there has been a flurry of 'skeletal stem cell' papers in the last few years, I consider this *Nature* paper to be the best of the bunch and certainly the most rigorous. Our students discussed this paper in their journal club and it was one of the most liked this past semester."

Reviewer B: "He is doing better than his peer group as he has already achieved a level of emerging national/international recognition at this stage of his career. There is no question, he will be involved in more journals and grant reviews when he becomes a senior faculty member."

Reviewer C: "Dr. Ono's research reputation cannot only be evidenced by his publication and funding record, but can also be observed by the number of invitations to present his research at major universities, research institutions, and international research meetings; many of which have led to award recognition by the International Bone and Mineral Society (IBMS) and the ASBMR. Dr. Ono is already an accomplished skeletal and dental biologist and a rising star in the skeletal and dental research fields."

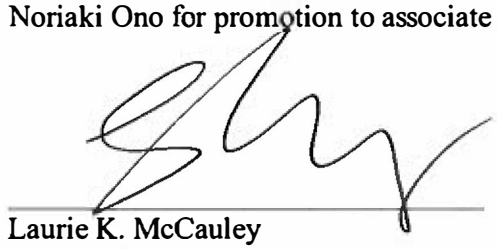
Reviewer D: "Dr. Ono is a dedicated, resourceful and broad thinking investigator... his work focuses on current and pressing questions and issues and is carried out with rigor and keen insight... Dr. Ono's studies remain at the forefront of biomedical research to which he continues to make timely and important contributions."

Reviewer E: "Dr. Ono's interest in skeletal stem cells is not restricted to bone marrow. Last year, he made another ground-breaking discovery by identifying PTHrP as the marker for the resting zone of the growth plate. The growth plate is responsible for longitudinal bone growth during the development stage. It has been known for a long time that the resting zone harbors the progenitors for growth plate chondrocytes, but no markers have been identified for those stem cells, thus hindering further research. In Dr. Ono's 2018 *Nature* article, he clearly demonstrated that PTHrP-positive cells in mouse growth plate continue to form columnar chondrocytes, undergo hypertrophy, and eventually become osteoblasts and stromal cells inside bone marrow. This is an extremely interesting finding because it unravels a type of stem cell that is initially unipotent and then acquires multi-potency at the post-mitotic stage. This idea has a fundamental impact on how we think about skeletal stem cells now. For this research, he was awarded an R01 last year and has several other R01 submissions under review."

Reviewer F: "In the Submitted Manuscripts section and the statement on scholarly activity, I was impressed with the perseverance demonstrated by Dr. Ono. He clearly has a strategy of publishing in high impact journals... I appreciated seeing his strategy for the very novel work on stromal cells

from the bone marrow, passing from one journal to another within the same journal family and then to different journals. Dr. Ono has a new R01, awarded in January 2018 that provides funding of $1,940,000. This grant is focused on stem cells in bone and has broad significance beyond oral health. I must say that this is a very impressive achievement, to have an R01 funded before reaching tenure."

Summary of Recommendation:
Professor Ono is a conscientious, dedicated teacher, brilliant scientist and well-rounded service contributor at the school, university, national and international levels. He has gained distinction in skeletal stem cell and bone regeneration and is a widely recognized innovator in the field of bone development research. Equally, his commitment to teaching and service parallels his research works as being exemplary. He is highly committed to the training of future professionals, both as a dentist-orthodontist and scientist. It is with the support of the Executive Committee, that I recommend Noriaki Ono for promotion to associate professor of dentistry, with tenure, School of Dentistry.



Laurie K. McCauley
Dean, School of Dentistry

May 2020