

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF ORTHOPAEDIC SURGERY
MEDICAL SCHOOL AND COLLEGE OF ENGINEERING
DEPARTMENT OF BIOMEDICAL ENGINEERING

Kenneth M. Kozloff, Ph.D., associate professor of orthopaedic surgery, with tenure, Department of Orthopaedic Surgery, Medical School, and associate professor of biomedical engineering, without tenure, Department of Biomedical Engineering, Medical School and College of Engineering, is recommended for promotion to professor of orthopaedic surgery, with tenure, Department of Orthopaedic Surgery, Medical School, and professor of biomedical engineering, without tenure, Department of Biomedical Engineering, Medical School and College of Engineering.

Academic Degrees:

Ph.D.	2005	University of Michigan
M.S.	2000	University of Michigan
B.S.E.	1997	University of Michigan

Professional Record:

2014-present	Associate Professor of Orthopaedic Surgery, with tenure, University of Michigan
2014-present	Associate Professor of Biomedical Engineering, University of Michigan
2008-2014	Assistant Professor of Biomedical Engineering, University of Michigan
2007-2014	Assistant Professor of Orthopaedic Surgery, University of Michigan

Summary of Evaluation:

Teaching: Dr. Kozloff is an excellent educator and mentor who has a positive impact on orthopaedic residents and future musculoskeletal scientists. He has actively participated in curriculum design and content delivery for the Department of Biomedical Engineering (BME 419/519), Medical School (M1 lectures), and Department of Orthopaedic Surgery Basic Science lectures for resident proficiency in required content. Additionally, Dr. Kozloff initiated, planned, and implemented a monthly virtual seminar series on topics related to exercise and sport science during the COVID pandemic. He actively mentors a multidisciplinary cohort of surgical residents, fellows, graduate, medical and undergraduate students. He has served on multiple graduate student thesis and research committees. His trainees have received numerous research awards for the quality of their work and have moved on to a variety of positions in industry and academia.

Research: Dr. Kozloff is a multi-disciplinary, team-oriented musculoskeletal scientist studying modulators of bone strength, fragility, and repair. He has developed novel imaging strategies for real-time, non-invasive assessment of bone mass, metabolism, and drug delivery. Dr. Kozloff's laboratory at the University of Michigan was the first to establish a novel treatment paradigm for osteogenesis imperfecta (OI), a rare skeletal fragility disease in which children can suffer fracture rates 10-fold higher than age-matched populations. Anti-resorptive bisphosphonates are the most

widely used intervention to prevent the high bone turnover and low bone mass associated with OI fragility. Dr. Kozloff's laboratory established a paradigm-shifting treatment strategy that changes the emphasis of therapy for OI from preventing bone destruction to increasing bone formation. The group was the first to demonstrate that antibodies to sclerostin, a negative inhibitor of bone formation, can induce anabolic signals in OI bone cells, and despite retention of the underlying causative genetic defect, can restore bone strength to non-diseased levels. Dr. Kozloff subsequently pursued multiple translationally focused studies that have provided new insight into clinical application and key safety outcomes for the application of this drug toward OI treatment. His research group has developed a novel, clinically relevant xenograft transplant model that may help bridge the gap between mouse and patient application. This work has had a significant, positive impact on the field, and has led to multiple industry partnerships from pharmaceutical companies interested in developing novel therapeutics for OI, including Mereo, Ultragenyx, Amgen, Mango Biotech. Furthermore, the outcomes of these studies have motivated several ongoing clinical trials evaluating this therapeutic strategy in OI patients. Based on this success and his expertise in the field, he was recently named chair of the 2023 OI Foundation annual scientific meeting.

In 2018, Dr. Kozloff expanded his research experience into human subject research to further define the underpinnings of skeletal fragility. He undertook a six-month sabbatical with the Michigan Performance Research Laboratory in the School of Kinesiology/Exercise and Sport Science Initiative. Here, he developed a new research collaboration with the Michigan Athletic Department to understand factors responsible for bone stress injuries in endurance runners. To better understand differences in individual training load across athletes and how this variability might contribute to injury, Dr. Kozloff has developed research in using wearable technology to quantify skeletal loading objectively. He was invited to participate in several workshops to expand this research focus, including the University of Michigan Biosciences Initiative-sponsored Ideas Lab (Predicting Human Performance), and the National Science Foundation-sponsored Engineering Research Visioning Alliance (Leveraging Biology to Power Engineering Impact). These efforts have led to new collaborative opportunities with industry partners focused on wearable technology, including Apple, Oura, and Samsung. Currently, the team is investigating wearable technology to monitor physiologic changes and skeletal adaptations in a large cohort of community-based runners.

Dr. Kozloff's work has resulted in 87 peer-reviewed publications and a robust, diversified research funding portfolio that highlights both his expertise as a principal investigator as well as his valuable team science and collaborative approach as co-investigator. Currently, he serves as the principal investigator or co-principal investigator on grants totaling over \$4M from the National Institutes of Health, Apple, Mango Biotech, the University of Michigan Biosciences Initiative, and the University of Michigan Department of Orthopaedic Surgery. Additionally, as a co-investigator, Dr. Kozloff contributes to studies exceeding \$9M in funding from the National Institutes of Health and the Department of Defense.

Recent and Significant Publications:

Matsushita Y, Nagata M, Kozloff KM, Welch JD, Mizuhashi K, Tokavanich N, Hallett SA, Link DC, Nagasawa T, Ono W, Ono N. A, "Wnt-mediated transformation of the bone marrow

stromal cell identity orchestrates skeletal regeneration,” *Nat Commun* 11(1): 332, 2020. PMID31949165/PMC6965122.

Surowiec RK, Battle LF, Ward FS, Schlecht SH, Khoury BM, Robbins C, Wojtys EM, Caird MS, Kozloff KM. “A xenograft model to evaluate the bone forming effects of sclerostin antibody in human bone derived from pediatric osteogenesis imperfecta patients,” *Bone* 130: 115118, 2020. PMID31678490/PMC6918492.

Scheiber AL, Barton DK, Khoury BM, Marini JC, Swiderski DL, Caird MS, Kozloff KM, “Sclerostin antibody-induced changes in bone mass are site specific in developing crania,” *Journal of Bone and Mineral Research* 34(12): 2301-2310, 2019. PMID31441963/PMC7458133.

Olvera D, Stolzenfeld R, Marini JC, Caird MS, Kozloff KM, “Low dose of bisphosphonate enhances sclerostin antibody-induced trabecular bone mass gains in *Brtl/+* osteogenesis imperfecta mouse model,” *Journal of Bone and Mineral Research* 33(7): 1272-1282, 2018. PMID29544018/PMC6084801.

Sinder BP, Salemi JD, Caird MS, Marini JC, Kozloff KM, “Rapidly growing *Brtl/+* mouse model of osteogenesis imperfecta improves bone mass and strength with sclerostin antibody treatment,” *Bone* 71: 115-23, 2015. PMID25445450/PMC4274252.

Service: Dr. Kozloff provides extensive service initiatives at the international, national, and institutional levels. These roles have included a four-year term on the Orthopaedic Research Society Board of Directors, chair of the Strategic Initiative Committee, member of the Fundraising Task Force, and member of the society’s Diversity and Inclusion Task Force. Currently, he serves as associate editor for *Connective Tissue Research*. Dr. Kozloff’s expertise is valued, and he has served on multiple peer review grant panels including for the National Institutes of Health (Skeletal Biology, Structure and Regeneration; Skeletal Biology, Disease and Development; High End Instrumentation Review; Special Emphasis SRG); National Science Foundation (Biomechanics and Mechanobiology) and Department of Defense (Military Operational Medicine Research Program). He has also performed additional ad hoc review services for the Osteogenesis Imperfecta Foundation, the Orthopaedic Research Education Foundation, the Washington University Musculoskeletal Research Center, and the City University of New York Research Foundation.

Dr. Kozloff not only provides outstanding leadership at the University of Michigan, but he gives back to the institution and the community. In 2018, he was selected to participate in the University of Michigan Road Scholar tour where he was able to firsthand see the challenges in our state, as well as the positive impacts that the university has made on society beyond the confines of our own institution. As the associate director, and now co-director of the University of Michigan Exercise and Sport Science Initiative (ESSI), he is dedicated to the mission to support and grow integrated and comprehensive sport- and exercise-related research and education at the University of Michigan. At ESSI he participated in strategic planning, developed novel funding lines, and attracted new industry sponsorships with companies including Apple, Oura, and Samsung. During the COVID-19 pandemic, he organized the virtual exercise and sport science seminar series which established new connections and research partnerships.

Within the Department of Orthopaedic Surgery, Dr. Kozloff serves as the associate director of the Functional Assessment core of a National Institutes of Health-sponsored P30 Core Center, where

he supports phenotypic characterization of a variety of animal models within the broad musculoskeletal community at Michigan and beyond. In addition, he serves on the departmental Finance Committee and Research Advisory Committee. He directs the department's internal Pilot and Feasibility grant program which supports high-quality scientific projects aimed at obtaining preliminary results to support applications for extramural support, and supports resident research within orthopaedic surgery. Dr. Kozloff has many years of valuable service to our department, the university, and musculoskeletal discovery.

External Reviewers:

Reviewer A: "Dr. Kozloff is an active member of Orthopedics Research Society, American Society for Bone and Mineral Research and Biomedical Engineering Society. Considering these activities and achievements Dr. Kozloff has been nationally and internationally recognized scientist in the research area of Bone and Orthopedics...My opinion is that Dr. Kozloff is a nationally and internationally recognized scientist that keeps an active and growing research program. His scientific record, publication record and educational commitments qualify him for a Professor position..."

Reviewer B: "I believe Dr. Kozloff has made significant contributions to the field of bone mechanics...Much of this work has been presented at national and international conferences... Dr. Kozloff's productivity and contributions to biomedical research would likely earn him tenure at my private institution that has an outstanding track record of extramural funding."

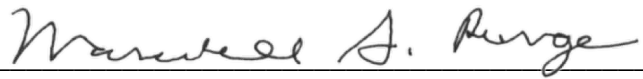
Reviewer C: "Dr. Kozloff and his trainees are very well respected in the 'Bone' community. He has been a significant contributor to the pursuit and investigation of pharmacologic treatment strategies and in the understanding of the skeletal biomechanics in osteogenesis imperfecta model systems...I have watched his continued trajectory of outstanding scholarly and scientific productivity. In fact, my students often present Dr. Kozloff's latest research manuscripts in our journal club meetings. His level of scientific rigor is commendable, and this is also one of the reasons I like for my group to read his manuscripts."

Reviewer D: "I can attest that Dr. Kozloff's work is very highly regarded by other specialists working on this condition, as his research is solid, thoughtful and of excellent methodological standard...He has contributed several more important studies on the effects of sclerostin inhibition in mouse models of osteogenesis imperfecta. Collectively, these reports are known as the 'Kozloff papers' in the field and are essential reading for anyone performing research on novel therapies of osteogenesis imperfecta."

Reviewer E: "Dr. Kozloff has consistently done excellent work that is internationally recognized for its rigor and impact...Dr. Kozloff ranks in the top tier of his peer group in academic musculoskeletal research...The breadth of his scholarship and his ability to attract sustained extramural funding from a range of sponsors is remarkable, as is his collaborative approach to research. Michigan has one of the strongest programs in musculoskeletal research in the US, and Dr. Kozloff is clearly an important contributor to the success of this program."

Summary of Recommendation:

Dr. Kozloff is making substantial contributions to the field of bone mechanics. He is an accomplished and highly distinguished musculoskeletal investigator with excellent funding and breadth of collaborations which makes him an outstanding candidate for promotion. He is highly regarded and often sought after by his peers and is recognized for his expertise in clinical care, education, and research. Therefore, I am pleased to recommend Kenneth M. Kozloff, Ph.D. for promotion to professor of orthopaedic surgery, with tenure, Department of Orthopaedic Surgery, Medical School, and professor of biomedical engineering, without tenure, Department of Biomedical Engineering, Medical School and College of Engineering.



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



Alec D. Gallimore, Ph.D.
Robert J. Vlasic Dean of Engineering
College of Engineering

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