BIOGRAPHICAL SKETCH

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NAME: Weaver, Samantha

eRA COMMONS USER NAME (credential, e.g., agency login): weaversr

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Wisconsin-Madison, Madison, WI, USA	B.S.	05/2014	Pre-Medicine, Spanish Literature, Women's Studies
University of Wisconsin-Madison, Madison, WI, USA	Ph.D.	05/2018	Endocrine and Reproductive Physiology
Mayo Clinic, Rochester, MN, USA	Postdoc	07/2023	Musculoskeletal Health

A. Personal Statement

I am an Assistant Professor in the Department of Comparative Biosciences at the University of Wisconsin-Madison School of Veterinary Medicine. I received a B.S. degree from the University of Wisconsin-Madison in 2014, then went on to complete a Ph.D. in mammary gland and lactation physiology at the University of Wisconsin-Madison in 2018. My postdoctoral work in the Mayo Clinic Department of Orthopedic Surgery was focused on characterizing novel molecular drivers of musculoskeletal disease, including PHLPP protein phosphatases and GIRK potassium channels. Musculoskeletal issues are the among the top reasons that people visit their doctors every day, yet there are limited therapies for osteoporosis, with significant side effects. There are no disease-modifying therapies for osteoarthritis. As an Assistant Professor, my research program seeks to define the basic molecular processes that govern bone and cartilage development and disease, with the goal of developing novel therapies to regenerate these tissues. I am an expert in pre-clinical rodent models of musculoskeletal disease, including surgical- and inflammation-induced osteoporosis and osteoarthritis. My lab uses a wide range of molecular biology techniques, both in vitro and in vivo, including transgenic mouse models, multi-omics, histomorphometry, and high-resolution imaging (μCT). An additional arm of my program studies the natural physiological processes that induce rapid bone loss, including pregnancy and lactation, as a model for aberrant bone loss later in life (i.e., postmenopausal osteoporosis).

Ongoing Research Support

R00AR080745 (PI: Samantha Weaver) 09/24/24-08/31/27
Title: Girk3 in bone biology and disease.
The goal of this grant is to characterize a novel target of bone remodeling called G protein gated inwardly-rectifying K+ channel 3 (Girk3), a key regulator of potassium flux and physiological processes. The central hypothesis is that Girk3 deletion enhances bone density in the adult skeleton by altering the secretion of IL-1B and other monocyte-derived cytokines that modify bone resorption.
Current Year Support: $249,000

Departmental Start-Up Funds (PI: Samantha Weaver) 09/16/24-09/16/29
Current Year Support: $150,000

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2024- Assistant Professor, Department of Comparative Biosciences, University of Wisconsin-Madison
2023-2024 Associate Consultant I, Mayo Clinic Department of Orthopedic Surgery
2021-2023 Senior Research Fellow, Mayo Clinic Department of Orthopedic Surgery
2018-2023 Postdoctoral Research Fellow, Mayo Clinic Department of Orthopedic Surgery
2014-2018 Graduate Research Assistant, University of Wisconsin-Madison Endocrinology and Reproductive Physiology Program

Honors

2023 Advances in Mineral Metabolism John Haddad Young Investigator Award
2022 American Society for Bone and Mineral Research Harold M. Frost Young Investigator Award
2021 Mayo Clinic Robert and Arlene Kogod Center on Aging Fellow
2021 Mayo Clinic Edward C. Kendall Fellow in Biochemistry
2020 Mayo Clinic Jennifer Jowsey, Ph.D. Award for Excellence in Research by a Research Fellow in Orthopedic Surgery
2020 American Society for Bone and Mineral Research Young Investigator Fund for Education and Research Award
2020 American Society for Bone and Mineral Research Plenary Poster Award
2020 Mayo Clinic 2020 Kelly Research Fellow in Orthopedics
2018 Top cited article in the Journal of Endocrinology
2018 Presidential Poster Competitor at ENDO 2018
2018 First place, Endocrine and Reproductive Physiology Oral Presentation Session
2017 First place, American Society of Nutrition Emerging Leaders in Nutrition Poster
2017 University of Wisconsin-Madison Graduate School Student Travel Research Grant
2017 Endocrine and Reproductive Physiology Travel Research Award
2016 Second place, Ph.D. Poster Competition at the Joint Annual Meeting of the American Dairy Science Association
2016 Abstract selected for oral presentation and press coverage at ENDO 2016
2016 National Science Foundation Graduate Research Fellowship
2015 College of Agricultural and Life Sciences W.D. Hoard Memorial Graduate Scholarship
2015 First place, Endocrine and Reproductive Physiology Poster Session
2015 Endocrine and Reproductive Physiology Program Graduate Student Research Award
2014 First place in the Undergraduate Original Research Paper Presentation at the Joint Annual Meeting of the American Dairy Science Association
2013 College of Agricultural and Life Sciences Study Abroad Award
2013 Cargill/Benevenga Undergraduate Research Stipend Recipient

C. Contributions to Science

1. **Modulation of serotonin metabolism in the prevention of hypocalcemia in dairy cattle.** My predoctoral training was conducted under Dr. Laura Hernandez at the University of Wisconsin-Madison. Dr. Hernandez shares joint appointments in the Department of Dairy Science, Department of Nutrition, and is a member of the Endocrine and Reproductive Physiology Program. Beginning in a dairy cow model, I first demonstrated that intravenous administration of a serotonin precursor (5-hydroxy-L-tryptophan; 5-HTP) immediately before parturition helped prevent cows from entering hypocalcemia, which can lead to other diseases or be fatal if left untreated. Elevating pre-partum serotonin concentrations increased calcium concentrations in part through elevated bone resorption, as dairy cows administered 5-HTP had increased concentrations of bone resorptive markers in their serum. I further went on to show that liver metabolism was affected by pre-partum administration of 5-HTP, showing improved whole-body adaptation to the onset of lactation in response to serotonergic modulation. The data from these projects comprised a successful application for the National Science Foundation Graduate Research Fellowship which supported my predoctoral training.

    a. Connelly MK, **Weaver SR**, Kuehnl JM, Fricke HP, Klister M, Hernandez LL. 2021. Elevated serotonin coordinates mammary metabolism in dairy cows. Physiol Rep 9: e14798.
    b. **Weaver SR**, Prichard AP, Endres EL, Newhouse SA, Peters TL, Crump PM, Akins MS, Crenshaw TD, Bruckmaier RM, Hernandez LL. 2016. Elevation of circulating serotonin improves calcium dynamics in the dairy cow transition period. J Endocrinology 230: 105-123.
    c. **Weaver SR**, Prichard AS, Prichard AP, Endres EL, Hernández-Castellano LE, Akins MS, Bruckmaier RM, Hernandez LL. 2017. Elevating serotonin pre-partum alters the Holstein dairy cow hepatic adaptation to lactation. PLoS One 12: e0184939.

2. **Serotonergic regulation of calcium and bone homeostasis during pregnancy and lactation.** Having established that serotonin is a central regulator of dairy cow calcium homeostasis, my focus turned towards the serotonin-calcium axis in human biomedical applications. Patients taking the class of antidepressants Selective Serotonin Reuptake Inhibitors (SSRI) have elevated intracellular serotonin concentrations. During

lactation, women mobilize significant amounts of calcium from the bone to support milk synthesis. While bone mass is thought to be completely recovered after weaning, my work showed that use of SSRIs during lactation increased mammary gland concentrations of serotonin, elevating the mammary gland production of parathyroid hormone-related protein (PTHrP), a potent stimulator of bone turnover. As such, mice administered SSRIs throughout pregnancy and lactation underwent extensive bone mobilization resulting in sustained reductions in bone mass up to nine months post-weaning. Additionally, my work showed that manipulation of the serotonergic axis through administration of SSRIs or through inhibition of serotonin signaling by inhibiting the rate limiting enzyme in serotonin synthesis (TPH1) negatively affected the bones of pups exposed throughout pregnancy and lactation. The projects concerning SSRIs and bone homeostasis formed the basis of an R01 that was funded just after my graduation.

a. **Weaver SR**, Fricke HP, Maerz NL, Vezina CM, Charles JF, Hernandez LL. 2018. Peripartum fluoxetine reduces maternal trabecular bone post-weaning and elevates mammary gland serotonin and PTHrP. Endocrinology 159(8): 2850-2862.
b. **Weaver SR**, Fricke HP, Xie C, Aiello RJ, Charles JF, Hernandez LL. 2018. Peripartum dietary supplementation of a small-molecule inhibitor of tryptophan hydroxylase 1 (TPH1) compromises infant, but not maternal, bone. Am J Physiol Endocrinol Metab 315(6): E1133-E1142.
c. **Weaver SR**, Fricke HP, Xie C, Charles JF, Hernandez LL. 2018. In utero and lactational exposure to the Selective Serotonin Reuptake Inhibitor fluoxetine compromises pup bones at weaning. Sci Rep 9(1): 238.
d. **Weaver SR,** Jury NJ, Gregerson KA, Horseman ND, Hernandez LL. 2017. Characterization of mammary-specific deletions for *Tph1* and *Lrp5* during murine lactation. Sci Rep 7: 15155.

3. **The role of PHLPPs and GIRKs in bone and cartilage development and repair.** I chose to conduct my postdoctoral research in the laboratory of Dr. Jennifer Westendorf at Mayo Clinic. My predoctoral work focused on whole-body physiology, specifically the endocrine signals that govern calcium and bone homeostasis during lactation. To support my development as an independent academic researcher, my attention turned to garnering skills in biochemistry and molecular biology. I chose to move into musculoskeletal health after attending national meetings in bone and cartilage and seeing the wide breadth of research and potential for clinical impact. The laboratory of Dr. Jennifer Westendorf proved to be an excellent environment in which to gain independence as a musculoskeletal researcher. As a postdoctoral fellow, I participated in several lines of research including: 1) the role of PHLPP phosphatases in cartilage development and homeostasis, 2) the role of GIRK ion channels in cartilage and bone development and disease, and 3) the sex-specific signals governing osteoarthritis development in males versus females.

a. **Weaver SR**, Torres HM, Arnold KM, Zars EL, Peralta-Herrera E, Taylor EL, Yu K, Marron Fernandez de Velasco E, Wickman K, McGee-Lawrence ME, Bradley EW, Westendorf JJ. 2024. Girk3 deletion increases osteoblast maturation and bone mass accrual in adult male mice. J Bone Miner Res Plus 8(10): ziae108.
b. Torres HM, Arnold KM, Oviedo M, Westendorf JJ, **Weaver SR**. 2023. Inflammatory processes affecting bone health and repair. Current Osteoporosis Reports 21(6): 842-853.
c. **Weaver SR**, Peralta-Herrera E, Torres HM, Jessen E, Bradley EW, Westendorf JJ. 2024. Phlpp1 alters the murine chondrocyte phospho-proteome during endochondral bone formation. Bone 189:117265.
d. **Weaver SR**, Taylor EL, Zars EL, Arnold KM, Bradley EW, Westendorf JJ. 2021. PH domain and leucine rich repeat phosphatase 1 (Phlpp1) suppresses parathyroid hormone receptor 1 (Pth1r) expression and signaling during bone growth. J Bone Miner Res 36(5): 986-999.
e. Taylor EL*, **Weaver SR***, Lorang IM, Arnold KM, Bradley EW, Fernandez de Velasco EM, Wickman K, Westendorf JJ. 2022. GIRK3 deletion facilitates kappa opioid signaling in chondrocytes, delays vascularization, and promotes bone lengthening in mice. Bone 159: 116391. *authors contributed equally

Complete List of Published Work in My Bibliography