
BIOGRAPHICAL SKETCH

Senior Trainer

NAME Laura L. Hernandez		POSITION TITLE Associate Professor	
eRA COMMONS USER NAME lauralorraine			
EDUCATION/TRAINING:			
INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
New Mexico State University, Las Cruces, NM	B.S.	December, 2002	Animal Science
New Mexico State University, Las Cruces, NM	M.S.	December, 2004	Animal Science/Toxicology
University of Arizona, Tucson, AZ	Ph.D.	May, 2008	Nutritional Sciences/Animal Science
University of Cincinnati, Cincinnati, OH	Post-Doc	June 2008- May 2011	Molecular and Cellular Physiology/Developmental Biology

A. Personal Statement

My research program is directed at better understanding how serotonin controls mammary gland development and physiology. I have authored 25 papers examining how serotonin is synthesized and metabolized in the mammary gland across three different species and have dissected the serotonin receptor subtypes present and some of their associated signaling mechanisms in regards to mammary gland development and physiology. I established that serotonin is responsible for governing calcium metabolism in the mother during lactation through regulation of parathyroid hormone related protein production in the mammary gland. My laboratory, was the first to establish that serotonin's regulation of parathyroid hormone related protein production was via the Hedgehog signaling pathway. We were able to establish the role of serotonin's regulation on Hedgehog signaling in collaboration with Drs. Lipinski and Vezina, co-investigators on this proposal. This has already proven a productive collaboration, with our recent publication describing a novel mechanism in which serotonin epigenetically regulates the expression of Sonic Hedgehog, resulting in pathway activation that drives the expression of PTHrP both in vitro and in vivo. Furthermore, we recently published data demonstrating a decrease in bone volume/total volume in the femurs of female mice that were on selective serotonin reuptake inhibitors during pregnancy and lactation compared to controls. Furthermore, we demonstrated that fetuses were also negatively affected, as demonstrated by reductions in bone volume as well as length compared to controls. This was performed using MicroCT analysis in conjunction with our new Co-I, Dr. Julia Charles from Brigham and Women's Hospital. The present application proposes to extend our work examining the effects of using selective serotonin reuptake inhibitors during pregnancy and lactation and how this may affect maternal bone density, and the possibility of developing a novel method to prevent this action through folic acid supplementation. As the present application focuses on contribution of serotonin, in particular mammary synthesized serotonin, on maternal health during pregnancy and lactation poises me to lead the project efforts as the principal investigator.

B. Positions and Honors

Positions and Employment:

2003-2004	Graduate Research Assistant, Department of Animal Science, College of Agriculture and Life Sciences, New Mexico State University, Las Cruces, NM. Mentor: Timothy T. Ross, Ph.D.
2005-2008	Graduate Research Assistant, Department of Animal Science, College of Agriculture and Life Sciences, University of Arizona, Tucson, AZ. Mentor: Robert J. Collier, Ph.D.
2008-2011	Postdoctoral Research Fellow, Department of Molecular and Cellular Physiology, College of Medicine, University of Cincinnati, Cincinnati, OH. Mentor: Nelson D. Horseman Ph.D.
2011-6/2017	Assistant Professor, Department of Dairy Science, College of Agriculture and Life Sciences, University of Wisconsin, Madison, WI.
7/2017	Associate Professor, Department of Dairy Science, College of Agriculture and Life Sciences
-present	University of Wisconsin, Madison, WI.

11/2017-present Associate Professor, Affiliate appointment, Department of Obstetrics and Gynecology, University of Wisconsin, School of Medicine and Public Health

Other Experience and Professional Memberships:

2005-present American Dairy Science Association
2011-present Endocrine Society
2012 Chair of Mammary Gland Biology Gordon Research Seminar
2012 Ad hoc reviewer, National Science Foundation
2011-present Ad hoc reviewer, Binational Agricultural Research and Development Fund
2014-present Editorial Board, Domestic Animal Endocrinology
2014-present Editorial Board, Journal of Dairy Science
2016-present Editorial Board, Journal of Animal Science
2014-present Lactation Biology Program Committee, American Dairy Science Association

Honors:

2003-2004 Minority Biomedical Research-Research Initiative for Scientific Enhancement Scholar (MBRS-RISE), NIH Biomedical Research Program, New Mexico State University
2004 Dean's Award of Excellence for a Graduate Student, New Mexico State University
2005-2008 NIH, Initiative for Maximizing Diversity (IMSD), University of Arizona
2008-2011 Ruth L. Kirschstein-NRSA Postdoctoral Trainee, CURE Fellow, University of Cincinnati
2012-2013 HHMI Junior faculty fellowship, University of Wisconsin
2014 Alfred Toepfer Faculty Fellow Award, College of Agriculture and Life Sciences, University of Wisconsin, Madison
2017 American Dairy Science Association, Foundation Scholar Award in Dairy Production
2018 Vilas Faculty Fellowship (2018-2019), University of Wisconsin

C. Contribution to Science

Serotonin was initially described to be produced by the mammary gland in 2004 by Dr. Nelson Horseman. As a graduate student I characterized the mammary serotonergic system in the bovine. To this end, I identified five unique serotonin receptor subtypes present in the bovine mammary gland and demonstrated that serotonin was important to regulating mammary gland function, and that each of the receptors likely regulates a different aspect of mammary gland function, physiology and metabolism.

1. **Hernandez, L.L.**, S.W. Limesand, J.L. Collier, N.D. Horseman, and R.J. Collier. 2009. The Bovine Mammary Gland Expresses Multiple Functional Isoforms of Serotonin Receptors. *J. Endocrinol.* 203:123-131. PMID:19654143.
2. **Hernandez, L.L.**, C.M. Stiening, J.B. Wheelock, L.H. Baumgard, A.M. Parkhurst, and R.J. Collier. 2008. Evaluation of Serotonin as a Feedback Inhibitor of Lactation in the Bovine. *J. Dairy Sci.* 91: 1834-1844. PMID:18420614.

2. Efforts during my post-doctoral training were focused on determining the physiological mechanisms within the mammary gland that were regulated by serotonin and which receptor subtype(s) through which the action was occurring. Additionally, efforts were focused on the use of selective serotonin reuptake inhibitors (SSRI) may influence mammary gland physiology and lactation. To this end, I demonstrated that SSRI treatment could induce tight junction disruption within the mammary gland and that this action was associated with signaling through the HTR7 subtype. Furthermore, it was demonstrated that women taking SSRI during pregnancy and lactation may have issues lactating that are attributed to serotonin's effects on tight junction closure at the onset of lactation.

1. **Hernandez, L.L.**, J. L. Collier, A.V. Vomachka, R. J. Collier, and N.D. Horseman. 2011. Suppression of lactation and acceleration of involution in the bovine by a selective serotonin reuptake inhibitor (SSRI). *J. Endocrinol.* 209:45-54. PMID:21307120.
2. Marshall, A.M., L.A. Nomssen-Rivers, **L.L. Hernandez**, K.G. Dewey, C.J. Chantry, K.A. Gregerson and N.D. Horseman. 2010. Intrinsic Serotonin Turnover Affects Mammary Epithelial Tight Junctions, and

Modulates Stage II Lactogenesis and Involution. *J. Clin. Endocrinol. Metab.* 95(2). 837-846. PMID:19965920.

3. Marshall, A. M., **L. L. Hernandez**, and N. D. Horseman. 2014. Serotonin and serotonin transport in the regulation of lactation. *J. Mammary Gland Biol. Neoplasia.* 19(1):139-146. PMID:24136337

3. Calcium homeostasis is intricately regulated in the mother, as calcium is the primary mineral component of milk. To this end, based on research illustrating the effects of serotonin and SSRI's on bone and calcium metabolism, I investigated the possibility that serotonin was critical to calcium homeostasis during lactation. The work performed in this area of focus has demonstrated that serotonin is responsible for the induction of parathyroid hormone related-protein in the mammary gland during lactation, which is the key hormone in regulated bone calcium release for the support of milk synthesis. Furthermore, it was shown that serotonin is critical for mammary gland calcium trafficking and the supplementation of serotonin precursors were able to increase release of calcium from bone and increase calcium secretion into milk. Finally, it was demonstrated that serotonin is capable of shifting use of transcriptional start sites within the SHH promoter and that this is the mechanism by which serotonin is influencing production of parathyroid hormone related-protein.

1. Weaver SR, Xie C, Charles JF, **Hernandez LL**. 2019. In utero and lactation exposure to the selective serotonin reuptake inhibitor fluoxetine compromises pup bones at weaning. *Sci. rep.* 9(1):238. PMID:30659249.
2. 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 compromises infant, but not maternal, bone. *Am. J. Endocrinol. Metab.* Oct 23. Epub ahead of print. PMID: 30351987.
3. Weaver SR, HP Fricke, C Xie, RJ Lipinski, CM Vezina, JF Charles, and **LL Hernandez**. 2018. Peripartum fluoxetine reduces maternal trabecular bone after weaning and elevates mammary gland serotonin and PTHrP. *Endocrinology.* 159(8):2850-2862. PMID:29893816.
4. Crenshaw, R. M. Bruckmaier, and **L. L Hernandez**. 2016. Elevating circulating serotonin improves calcium dynamics in the peripartum dairy cow. *J. Endocrinol.* 230(1):105-123.

Complete List of Published Work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/1NqEvwdYmug5a/bibliography/47294718/public/?sort=date&direction=ascending>.

D. Research Support

Ongoing Research Support

R01HD094759 Hernandez (PI) 7/20/2018-4/30/2023
NIH/NICHD
"Influence of SSRI use during pregnancy and lactation on maternal bone health"

2016-67015-24584 Hernandez (PI) 1/1/2016-12/31/2020
USDA, AFRI Foundation Grant
"Serotonin modulates calcium homeostasis by mammary production of parathyroid hormone related-protein"

WIS01857 Hernandez (PI) 9/1/2015-8/31/2019
USDA, HATCH Multi-State Research Formula Fund
"Effects of increasing residual milk and milking frequency on lactation physiology, milk yield, milking time, and teat tissue stress"

WIS02099 Hernandez (PI) 10/1/2019-9/30/2023
USDA, HATCH Formula Fund
"Determination of Optimal Calcium Status in Peripartum Dairy Cow for Optimal Long-Term Health and Production Outcomes"

58-5090-9-019F Hernandez (Co-PI) 3/1/2019-2/28/2022
Canola Council of Canada

“Utilization of Canola Meal in the Diets of Early Lactation Dairy Cows”

Previous Research Support

WIS01732 Hernandez (PI) 9/1/2013-8/31/2018
USDA, HATCH Formula Fund
“Calcium Homeostasis in Dairy Cattle”

2013-67015-21348 Hernandez (Co-PI) 10/1/2013-6/30/2018
USDA, AFRI Foundation Grant
“Application of metagenomic techniques to diagnosis and prevention of bovine mastitis”

WIS01618 Hernandez (PI) 06-01-2011 – 08-31-2013
USDA, HATCH Formula Fund
“Calcium Homeostasis in Dairy Cattle”

This project was focused on determining the mechanism by which serotonin induced parathyroid hormone related protein production in the mammary gland to modulate bone calcium mobilization during lactation.

MSN175895 Hernandez (PI) 7/1/2014-6/30/2015
UW-Madison, Graduate School Annual Competition,
“Role of Serotonin in Regulating Calcium Mobilization During the Early Peri-Partum Period”

Hernandez (PI) 7/1/2014-6/30/2016
UW Consortium for Extension and Research in Agriculture and Natural Resources (CERANR)
“Use of 5-hydroxy-L-tryptophan as a modulator of hypocalcemia in transition dairy cattle”