
BIOGRAPHICAL SKETCH

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NAME Laura L. Hernandez		POSITION TITLE Assistant Professor	
eRA COMMONS USER NAME lauralorraine			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as			
INSTITUTION AND LOCATION	DEGREE (if applicable)	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

Throughout my graduate and post-doctoral training and as an independent investigator my research program has been directed at better understanding how serotonin controls mammary gland development, maternal physiology during lactation, and the synthesis of milk at a molecular level. As an Assistant Professor, I have authored 20 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 just received tenure November 4, 2016 through the Biological Division at the University of Wisconsin-Madison. 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 Dr. Vezina, co-investigators on a R01 proposal currently under review. As a post-doctoral fellow, I additionally became interested in how onset of stage II lactogenesis occurs in obese women and often results in failure of breastfeeding for the infant. There has been little effort focused on the mechanisms underlying the defects that may be present in the mammary tissue that are attributed to the obese condition. Serotonin has been reported to be elevated in obese individuals. Furthermore, our group has shown that at high concentrations serotonin can disrupt tight junctional complexes in the mammary gland, which is a hallmark of involution of the mammary gland. I was able to demonstrate that serotonin is also elevated in mammary glands collected from obese rats, as were markers of inflammation. A recent MD trainee in my laboratory published data demonstrating that peripheral serotonin deficiency during high-fat diet feeding reduced pup mortality, mammary gland inflammation, and improved lactation on days 0-2. 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. In addition to my research roles, I am on the editorial boards of Domestic Animal Endocrinology, Journal of Dairy Science, and the Journal of Animal Science. Furthermore, my documented collaborations with Dr. Vezina set the stage for a successful collaboration on this project and the mentorship of Adrienne Cheng.

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-present Assistant Professor, Department of Dairy Science, College of Agriculture and Life Sciences, University of Wisconsin, Madison, WI.

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
- 2016-present American Society of Nutrition

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
- Nov 2015 Associate Professor with Tenure, Biological Division of the University of Wisconsin-Madison

C. Contribution to Science

1. 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.

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.

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. Finally, I demonstrated that high-fat diet feeding of rats resulted in increased serotonin production by the mammary gland and disrupted junctional complexes.

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.

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.

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.

Hernandez L.L., B.E. Grayson, E. Yadav, R.J. Seeley, and N.D. Horseman. 2012. High fat diet alters lactation outcomes: possible involvement of inflammatory and serotonergic pathways. *PLoS One.* 7(3):e32598. PMID:22403677.

3. Maternal homeostasis is critical to the synthesis of milk by the mammary gland. Maternal nutrition is an important component of milk synthesis during lactation and can influence productivity by the mammary gland, as well as negatively impact maternal physiological status during this precarious time. 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. In addition to calcium homeostasis, maternal energy status during lactation is critical to successful production of milk. Serotonin has been demonstrated to effect glucose metabolism at both the level of the liver and pancreas during pregnancy. Therefore, we have also focused our efforts on the role of serotonin on milk synthesis during consumption of high fat diets.

Weaver, S.R., J.C. Bohrer, A.S. Prichard, P.K. Perez, L.J. Streckenbach, J.M. Olson, M.E. Cook, and **L.L. Hernandez**. 2016. Serotonin deficiency rescues lactation on day 1 in mice fed a high fat diet. *PLoS One.* 11(9):e0162432.

Weaver, S. R., A. P. Prichard, E. L. Endres, S. A. Newhouse, T. L. Peters, P. M. Crump, M. S. Akins, T. D. 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. PMID: 27390301.

Laporta, J., F. Peñagaricano, and **L. L. Hernandez**. 2015. Transcriptomic analysis of the mouse mammary gland reveals new insights for the role of serotonin in lactation. *PLoS One.* 10(10):e0140425. PMID:26470019.

Laporta, J., S.A. Moore, S. R. Weaver, C. M. Cronick, M. Olsen, A. P. Prichard, B. P. Schnell, T. D. Crenshaw, F. Peñagaricano, R. M. Bruckmaier, and **L. L. Hernandez**. 2015. Increasing serotonin concentrations alter calcium and energy metabolism in dairy cows. *J. Endocrinol.* 226(1):43-55. PMID: 26099356.

Laporta, J., K. P. Keil, C. M. Vezina, and **L. L. Hernandez**. 2014. Peripheral serotonin regulates maternal calcium trafficking in mammary epithelial cells during lactation in mice. *PLoS One.* 9(10):e110190. PMID:2529912.

Laporta, J., K. Keil, S. R. Weaver, C. Cronick, A. P. Prichard, T. D. Crenshaw, G. Heyne, C. M. Vezina, R. J. Lipinski, and **L. L. Hernandez**. 2014. Serotonin regulates calcium homeostasis in lactation by epigenetic activation of Hedgehog signaling. *Mol. Endocrinol.* 28(11):1866-1874. PMID: 25192038.

Horseman N. D., Hernandez L. L. 2014. New Concepts of Breast Cell Communication to Bone. *Trends Endocrinol. Metab.* 25(1):34-41. PMID:24055165.

Laporta, J., T. L. Peters, S. R. Weaver, K. E. Merriman and **L. L. Hernandez**. 2013. Feeding 5-hydroxy-L-tryptophan during the transition from pregnancy to lactation increases calcium mobilization from bone in rats. *Dom. Anim. Endocrinol.* 44(4):176-184. PMID:23733710.

Hernandez, L.L., K.A. Gregerson, and N.D. Horseman. 2012. Serotonin is an upstream regulator in the breast-to-bone axis. *Am. J. Physiol. Endocrinol. Metab.* 302:E1009-E1015. PMID:22318950.

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

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”

WIS01732 Hernandez (PI) 9/1/2013-8/31/2018

USDA, HATCH Formula Fund

“Calcium Homeostasis in Transition Dairy Cows”

2013-67015-21348 Hernandez (Co-PI) 10/1/2013-9/30/2017

USDA, AFRI Foundation Grant

“Application of metagenomic techniques to diagnosis and prevention of bovine mastitis”

Previous Research Support

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.