BIOGRAPHICAL SKETCH

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NAME: Lei Wang

POSITION TITLE: Postdoctoral Research Associate

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Zhengzhou University, China	Bachelor of Medicine	07/2011	Clinical Medicine
University of Florida, Gainesville, FL, USA	Ph.D.	08/2016	Pharmacodynamics

A. Personal Statement

Initially, my career goal was to become a clinician; however, this career pathway was altered when I started clinical internships during my final year in the Medical School of Zhengzhou University. In the clinical settings, I saw patients died of hypertension-related cardiovascular diseases. Most of these cardiovascular diseases could have been prevented if their blood pressure was under control but several of the patients had resistant hypertension. To better understand the pathophysiology causing hypertension and to seek novel therapeutics for hypertension, I applied and was accepted to the Graduate Program in Pharmacodynamics at the University of Florida. During the Ph.D. training, I studied the neural mechanisms behind the stress-induced diseases such as anxiety and hypertension under the mentorship of Dr. Eric Krause. After graduation, I joined the laboratories of Dr. Steve Mifflin and Dr. J. Thomas Cunningham to study the central pathways involved in sleep apnea induced hypertension. My current research focuses on investigating how CRH-producing neurons that project from the paraventricular nucleus of the hypothalamus to the nucleus of the solitary tract contribute to intermittent hypoxia induced hypertension.

B. Positions and Honors

Positions

Aug 2011 – Aug 2016 Graduate Assistant
Department of Pharmacodynamics
University of Florida, Gainesville, FL

Sep 2016 – Present Postdoctoral Research Associate
Department of Physiology & Anatomy
University of North Texas Health Science Center, Fort Worth, Texas

Honors

2007 **Outstanding Undergraduate Student Scholarship**, Zhengzhou University, China

2011 **Alumni Graduate Fellowship**, University of Florida

2014 **Best Poster Award**, Graduate Student Division, 27th Annual Research Showcase, College of Pharmacy, University of Florida

2015 **Best Poster Award**, Graduate Student Division, 28th Annual Research Showcase, College of Pharmacy, University of Florida

2015 **Best Poster Award**, Graduate Student Category, 5th Annual North Central Florida Society for Neuroscience Chapter Conference and Brain Awareness Week

2015 21st Annual **Outstanding International Student Award**, University of Florida

2016 **Oral Competition Finalist (Top 3)**, 29th Annual Research Showcase, College of Pharmacy, University of Florida

2016 **Selected to Represent the Pharmacodynamics Department** for the 1st Annual Graduate Student Appreciation Week, University of Florida

2017 **Postdoctoral Travel Award (2016-2017)**, Graduate School of Biomedical Sciences, University of North Texas Health Science Center

2017 **Physiological Genomics Interest Group New Investigator Award,** American Physiological Society

2017 **Postdoctoral Travel Award (2017-2018)**, Graduate School of Biomedical Sciences, University of North Texas Health Science Center

2017 **Onsite Poster Presentation Award: Post Doctorate,** American Heart Association Council on Hypertension

Society Membership

American Heart Association
American Physiological Society

C. Contribution to Science

1. My graduate research focused on studying how the angiotensin type 1a receptor (AT_{1a}) in the paraventricular nucleus of the hypothalamus (PVN) regulates stress responses and cardiovascular functions. We have found that optogenetic excitation of AT_{1a}-expressing neurons in the PVN activated the hypothalamic-pituitary-adrenal (HPA) axis and increased blood pressure, while optogenetic inhibition of AT_{1a}-expressing neurons in the PVN attenuated the behavioral and HPA axis responses to stress. Deletion of AT_{1a} from PVN neurons decreased behavioral, neuroendocrine, and cardiovascular responses to stress.

- **Wang L**, Hiller H, Smith JA, de Kloet AD, Krause EG. Angiotensin type 1a receptors in the paraventricular nucleus of the hypothalamus control cardiovascular reactivity and anxiety-like behavior in male mice. Physiological Genomics. 2016.
- de kloet AD, **Wang L* (co-first author)**, Pitra S, Hiller H, Smith JA, Tan Y, Nguyen D, Cahill KM, Sumners C, Stern JE, Krause EG. A Unique 'Angiotensin Sensitive' Neuronal Population Coordinates Neuroendocrine, Cardiovascular and Behavioral Responses to Stress. Journal of Neuroscience. 2017

2. Another line of my graduate research was to study the anti-stress and cardiovascular-protective effects of angiotensin converting enzyme 2 (ACE2). ACE2 is a key enzyme which converts angiotensin-II into angiotensin-(1-7). We have found that ACE2 overexpression or pharmacological activation of ACE2 in the brain decreased the anxiety-like behavior and activation of the hypothalamic-pituitary-adrenal axis in mice. The anxiolytic effect of ACE2 is mediated by the activation of mas receptors in the brain which promotes the GABAergic

transmission within the basolateral amygdala. ACE2 also acts in the periphery to reduce inflammation and protect against myocardial infarction induced cardiac dysfunction.

- Qi YF, Zhang J, **Wang L**, Shenoy V, Krause E, Oh SP, Pepine CJ, Katovich MJ, Raizada MK. Angiotensin-converting enzyme 2 inhibits high-mobility group box 1 and attenuates cardiac dysfunction post-myocardial ischemia. J Mol Med (Berl). 2015.
- **Wang L**, de kloet AD, Pati D, Hiller H, Smith JA, Pioquinto DJ, Ludin JA, Oh SP, Katovich MJ, Raizada MK, Frazier CJ, Krause EG. Angiotensin converting enzyme 2 decreases anxiety-like behavior by acting on mas receptor in the brain. Neuropharmacology. 2016.
- **Wang LA**, de Kloet AD, Smeltzer MD, Cahill KM, Hiller H, Bruce EB, Pioquinto DJ, Ludin JA, Katovich MJ, Raizada MK, Krause EG. Coupling Corticotropin-Releasing-Hormone and Angiotensin Converting Enzyme 2 Dampens Stress Responsiveness in Male Mice. Neuropharmacology. 2018.

3. I have contributed to a research project led by Dr. Annette de Kloet investigating the role of central renin-angiotensin system in diet-induced obesity. This project revealed that the AT_{1a} within the PVN is involved in the high-fat diet induced neuroinflammation, obesity, and hypertension.

- de Kloet AD, Pati D, **Wang L**, Hiller H, Sumners C, Frazier CJ, Seeley RJ, Herman JP, Woods SC, Krause EG. Angiotensin type 1a receptors in the paraventricular nucleus of the hypothalamus protect against diet-induced obesity. J Neurosci. 2013.
- de Kloet AD, Pioquinto DJ, Nguyen D, **Wang L**, Smith JA, Hiller H, Sumners C. Obesity induces neuroinflammation mediated by altered expression of the renin-angiotensin system in mouse forebrain nuclei. Physiol Behav. 2014.

4. The brain renin-angiotensin system is heavily involved in the regulation of stress responsiveness and cardiovascular function. The majority of studies focus on the angiotensin type 1 receptor (AT_{1a}) while little attention has been paid to the angiotensin type 2 receptor (AT_2) because this receptor was previously thought to have low levels of expression in the adult brain. However, our study found that AT_2 is expressed in neurons in brain regions regulating metabolism, cardiovascular function, and stress responsiveness. Further study revealed that AT_2 is expressed in GABAergic neurons that innervate PVN vasopressin neurons and activation of AT_2 increases the inhibitory inputs to vasopressin neurons and decreases blood vasopressin levels.

- de Kloet AD, **Wang L**, Ludin JA, Smith JA, Pioquinto DJ, Hiller H, Steckelings UM, Scheuer DA, Sumners C, Krause EG. Reporter mouse strain provides a novel look at angiotensin type-2 receptor distribution in the central nervous system. Brain Struct Funct. 2016.
- de Kloet AD, Pitra S, **Wang L**, Hiller H, Pioquinto DJ, Smith JA, Sumners C, Stern JE, Krause EG. Angiotensin Type-2 Receptors Influence the Activity of Vasopressin Neurons in the Paraventricular Nucleus of the Hypothalamus in Male Mice. Endocrinology. 2016.

5. I have also contributed to a research project investigating the neural mechanisms underlying the anxiolytic effects associated with acute hypernatremia. This line of research revealed that acute hypernatremia elicited the release of endogenous oxytocin, which attenuated anxiety by altering hypothalamic and limbic neuronal activity.

- Frazier CJ, Pati D, Hiller H, Nguyen D, **Wang L**, Smith JA, MacFadyen K, de Kloet AD, Krause EG. Acute hypernatremia exerts an inhibitory oxytocinergic tone that is associated with anxiolytic mood in male rats. Endocrinology. 2013.

- Smith JA, **Wang L**, Hiller H, Taylor CT, de Kloet AD, Krause EG. Acute hypernatremia promotes anxiolysis and attenuates stress-induced activation of the hypothalamic-pituitary-adrenal axis in male mice. Physiol Behav. 2014.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/46309049/?sort=date&direction=descending

Peer Reviewed Publications:

1. de Kloet AD, Pati D, **Wang L**, Hiller H, Sumners C, Frazier CJ, Seeley RJ, Herman JP, Woods SC, Krause EG. Angiotensin type 1a receptors in the paraventricular nucleus of the hypothalamus protect against diet-induced obesity. J Neurosci. 2013.
2. Frazier CJ, Pati D, Hiller H, Nguyen D, **Wang L**, Smith JA, MacFadyen K, de Kloet AD, Krause EG. Acute hypernatremia exerts an inhibitory oxytocinergic tone that is associated with anxiolytic mood in male rats. Endocrinology. 2013.
3. Smith JA, **Wang L**, Hiller H, Taylor CT, de Kloet AD, Krause EG. Acute hypernatremia promotes anxiolysis and attenuates stress-induced activation of the hypothalamic-pituitary-adrenal axis in male mice. Physiol Behav. 2014.
4. de Kloet AD, Pioquinto DJ, Nguyen D, **Wang L**, Smith JA, Hiller H, Sumners C. Obesity induces neuroinflammation mediated by altered expression of the renin-angiotensin system in mouse forebrain nuclei. Physiol Behav. 2014.
5. Smith JA, Pati D, **Wang L**, de Kloet AD, Frazier CJ, Krause EG. Hydration and beyond: neuropeptides as mediators of hydromineral balance, anxiety and stress-responsiveness. [Review]. Frontiers in Systems Neuroscience. 2015.
6. Qi YF, Zhang J, **Wang L**, Shenoy V, Krause E, Oh SP, Pepine CJ, Katovich MJ, Raizada MK. Angiotensin-converting enzyme 2 inhibits high-mobility group box 1 and attenuates cardiac dysfunction post-myocardial ischemia. J Mol Med (Berl). 2015.
7. de Kloet AD, **Wang L**, Ludin JA, Smith JA, Pioquinto DJ, Hiller H, Steckelings UM, Scheuer DA, Sumners C, Krause EG. Reporter mouse strain provides a novel look at angiotensin type-2 receptor distribution in the central nervouas system. Brain Struct Funct. 2016.
8. **Wang L**, de kloet AD, Pati D, Hiller H, Smith JA, Pioquinto DJ, Ludin JA, Oh SP, Katovich MJ, Raizada MK, Frazier CJ, Krause EG. Angiotensin converting enzyme 2 decreases anxiety-like behavior by acting on mas receptor in the brain. Neuropharmacology. 2016.
9. de Kloet AD, Pitra S, **Wang L**, Hiller H, Pioquinto DJ, Smith JA, Sumners C, Stern JE, Krause EG. Angiotensin Type-2 Receptors Influence the Activity of Vasopressin Neurons in the
   Paraventricular Nucleus of the Hypothalamus in Male Mice. Endocrinology. 2016.
10. **Wang L**, Hiller H, Smith JA, de Kloet AD, Krause EG. Angiotensin type 1a receptors in the paraventricular nucleus of the hypothalamus control cardiovascular reactivity and anxiety-like behavior in male mice. Physiological Genomics. 2016.
11. de kloet AD, **Wang L* (co-first author)**, Pitra S, Hiller H, Smith JA, Tan Y, Nguyen D, Cahill KM, Sumners C, Stern JE, Krause EG. A Unique 'Angiotensin Sensitive' Neuronal Population Coordinates Neuroendocrine, Cardiovascular and Behavioral Responses to Stress. Journal of Neuroscience. 2017
12. Peris J, Macfadyen K, Smith JA, de Kloet AD, **Wang L**, Krause EG. Oxytocin receptors are expressed on dopamine and glutamate neurons in the mouse ventral tegmental area that project to nucleus accumbens and other mesolimbic targets. Journal of Comparative Neurology. 2017.

13. **Wang LA**, de Kloet AD, Smeltzer MD, Cahill KM, Hiller H, Bruce EB, Pioquinto DJ, Ludin JA, Katovich MJ, Raizada MK, Krause EG. Coupling Corticotropin-Releasing-Hormone and Angiotensin Converting Enzyme 2 Dampens Stress Responsiveness in Male Mice. Neuropharmacology. 2018.

Abstracts and Poster Presentations Served as First-Authors:

1. **Wang L**, de Kloet AD, Hiller H, Nguyen D, Smith JA, Krause EG. Angiotensin Converting Enzyme 2 is anxiolytic, alters stress-induced neuronal activation and expression of inflammatory cytokines in mice. The Society for Neuroscience Annual Conference. 2013.
2. **Wang L**, de Kloet AD, Pati D, Hiller H, Smith JA, Pioquinto DJ, Oh SP, Katovich MJ, Raizada MK, Frazier CJ, Krause EG. Increasing Angiotensin Converting Enzyme 2 Activity in the Brain Is Anxiolytic and Dampens Activation of Hypothalamic-Pituitary-Adrenal Axis in Male Mice. Experimental Biology. 2015.
3. **Wang L**, de Kloet AD, Pati D, Hiller H, Smith JA, Pioquinto DJ, Oh SP, Katovich MJ, Raizada MK, Frazier CJ, Krause EG. Angiotensin converting enzyme 2 attenuates the behavioral and endocrine responses to stress by acting on mas receptors in the brain. Society for Behavioral Neuroendocrinology Conference. 2015.
4. **Wang L**, de Kloet AD, Smith JA, Hiller H, Sumners C, Raizada MK, Krause EG. Angiotensin type 1a receptors within the paraventricular nucleus of hypothalamus regulate cardiovascular and behavioral responsiveness to psychological stress. Experimental Biology. 2016.
5. **Wang L**, de Kloet AD, Hiller H, Smith JA, Ludin JA, Pioquinto DJ, Oh SP, Sumners C, Katovich MJ, Raizada MK, Krause EG. Bi-directional regulation of stress responsiveness by the local renin angiotensin system in the paraventricular nucleus of hypothalamus. Neurobiology of Stress Workshop. 2016.
6. **Wang L**, Mifflin S. Chronic Intermittent Hypoxia Decreases the Levels of Corticotropin-Releasing Hormone Receptor 2 in the Nucleus of the Solitary Tract in Rats. Experimental Biology. 2017.
7. **Wang L**, Mifflin S. Intermittent Hypoxia Attenuates Corticotropin-Releasing Hormone Receptor 2 (CRHR2) mRNA and CRHR2-Mediated Calcium Influx in Neurons in the Nucleus of the Solitary Tract. American Heart Association Council on Hypertension. 2017.
8. **Wang L,** Nguyen D, Cross S, Mifflin S. Corticotropin-Releasing Hormone Receptor 2 in the Nucleus of the Solitary Tract Contributes to the Intermittent Hypoxia Induced Hypertension. Experimental Biology Abstracts. 2018.

D. Research Support

July 2018 – June 2020 Postdoctoral Fellowship, American Heart Association
Total Amount: $104,060
Percentile Rank: 0.14%
Pay Line: 28.79%