BIOGRAPHICAL SKETCH

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NAME: Marsha Louise Pierce

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

POSITION TITLE: Principal Investigator

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
Creighton University, Omaha, NE, USA	B.S.	12/2002	Biology
Creighton University, Omaha, NE, USA	M.S.	12/2008	Biomedical Sciences
Creighton University, Omaha, NE, USA	Ph.D.	05/2015	Biomedical Sciences
Creighton University, Omaha, NE, USA	Postdoctoral Fellowship	6/2019	Pharmacology

A. Personal Statement

I perform and direct neuropharmacological research studying the effects of marine natural products and oxytocin (OT) analogs on cellular signaling, neurite outgrowth, and neurotoxicity in murine primary neuronal cultures and human-derived *in vitro* neuronal-like cell lines, which will ultimately help us understand structural and functional effects of these compounds to inform neuroscience drug development. These neuroactivity screenings include high throughput *in vitro* functional assays, such as calcium mobilization and FLIPR membrane potential (FMP, a surrogate for K^+ channel function) which are routinely performed in my laboratory. Previously, I have characterized oxytocin and vasopressin analogs in Chinese hamster ovary (CHO) cells expressing oxytocin receptor or vasopressin receptor 1a from marmoset, titi monkey, macaque and/or human. However, heterologous systems differ from intact neurons, and cellular context is crucial for understanding GPCR signaling profiles. Thus, I have acquired a mouse model that expresses green fluorescent protein under the control of the oxytocin receptor promoter, which we are currently assessing for sexually dimorphic expression patterns in the brain and plan to use for behavioral experiments with novel oxytocin analogs. I have also previously characterized effects of the marine natural product Brevetoxin in a murine photothrombotic stroke model to assess functional post-stroke recovery. Relevant publications include:

1. Sequeira E, **Pierce ML**, Akasheh D, Sellers S, Gerwick WH, Baden DG, Murray TF. (2020). Epicortical Brevetoxin Treatment Promotes Neural Repair and Functional Recovery after Ischemic Stroke. Marine drugs. 21 July 2020 https://doi.org/10.3390/md18070374
2. **Pierce ML**, French JA, Murray TM. (2020). Comparison of the pharmacologic profiles of arginine vasopressin and oxytocin analogs at marmoset, macaque, and human vasopressin 1a receptors. Biomed Pharmacother. Biomed Pharmacother. 2020 Jun;126:110060.
3. **Pierce ML**, French JA, Murray TM. (2020). Comparison of the pharmacologic profiles of arginine vasopressin and oxytocin analogs at marmoset, titi monkey, macaque, and human oxytocin receptors. Biomed Pharmacother. 2020 May;125:109832.
4. Li Y, Yu H, Zhang Y, Leao T, Glukhov E, **Pierce ML**, Zhang C, Kim H, Mao HH, Fang F, Cottrell GW, Murray TF, Gerwick L, Guan H, Gerwick WH. (2020). Pagoamide A, a cyclic depsipeptide isolated for a cultured marine chlorophyte, Debesia sp., using MS/MS-based molecular networking. J Nat Prod. 2020 Jan 9. doi: 10.1021/acs.jnatprod.9b01019. PMID: 31916778

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2019— Assistant Professor, Midwestern University, Department of Pharmacology, College of Graduate Studies
2015—2019 Postdoctoral Fellow, Creighton University, Department of Pharmacology, School of Medicine
2011—2015 Graduate Fellow, Creighton University, Department of Biomedical Sciences, School of Medicine
2006—2008 Graduate Fellow, Creighton University, Department of Biomedical Sciences, School of Medicine
2005—2011 Research Technician III, Creighton University, Department of Biomedical Sciences, School of Medicine

Professional Memberships

2020—present Member, Cognitive Science Society
2019—present National Faculty, National Board of Osteopathic Medical Examiners
2018—present Member, American Society for Pharmacology and Experimental Therapeutics
2015—present Member, Society for Neuroscience
2009—present Member, Association for Research in Otolaryngology

Honors and Awards

2021 Science, Technology, and Environment Policy Advisory Council for the 117th Congress
2020 Society for Neuroscience Early Career Policy Ambassadors Program
2015 First Place Award in Oral Presentation, Graduate Student, Midwest Student Biomedical Research Forum
2013 Best Oral Presentation, St. Albert's Day University Research Forum
2012—2015 Creighton University Graduate Student Government Student Travel Award
2011—2015 Creighton University Department of Biomedical Sciences Graduate Student Stipend
2007 Keystone Symposia Travel Award
2007 Creighton Student Travel Award

C. Contributions to Science

1. With the relatively recent discovery of microRNAs, I was fortunate to participate in pioneering research regarding microRNAs in the ear field. While pursuing my Master's degree, I was an author on the first publication establishing that microRNAs are expressed in the mouse inner ear and likely contribute to inner ear development and function. Results from this analysis lead us to focus on a particular microRNA gene family that displayed a sensory cell-specific expression pattern. In our next publication, we established that this family of microRNAs was conserved in sensory cells across a broad range of organisms throughout the phylogenetic tree. Results from our conservation analysis strengthened our hypothesis that microRNAs are integral to inner ear development, maintenance and function, and led us toward functional studies to address microRNA roles in development. To examine these functional roles, I generated the first conditional knockout of microRNAs in the mouse inner ear, which demonstrated that microRNAs are required for normal inner ear development and innervation. We then refined our knockout system to focus specifically on hair cells. For my Ph.D. research, I acquired knockout mouse models from this neurosensory microRNA-183 family and demonstrated knockout-specific age-related hair cell and sensorineural defects and identified several genes that may contribute to the observed phenotype. Additionally, collaboration with Dr. Michael Weston in the School of Dentistry at Creighton University on a microRNA-183 family misexpression model (expressed in supporting cells) demonstrates progressive hearing loss and neurosensory hair cell loss, validating the importance cellular-specific microRNA targeting.
    a. Banks SA, **Pierce ML**, Soukup GA. (2019). Sensational microRNAs: Neurosensory roles of the microRNA-183 family. Mol Neurobiol. 2019 Jul 29. doi: 10.1007/s12035-019-01717-3. Review. PMID: 31359323
    b. Weston MD, Tarang S, **Pierce ML,** Pyakurel U, Rocha-Sanchez SM, McGee J, Walsh EJ, Soukup GA. (2018). A mouse model of miR-96, miR-182 and miR-183 misexpression implicates miRNAs in cochlear cell fate and homeostasis. Sci Rep. 2018 Feb 23;8(1):3569. doi: 10.1038/s41598-018-21811-1. PMID: 29476110

c. Weston MD, **Pierce ML**, Jensen-Smith HC, Fritzsch B, Rocha-Sanchez S, Beisel KW, Soukup GA. (2011) MicroRNA-183 family expression in hair cell development and requirement of microRNAs for hair cell maintenance and survival. Dev Dyn. 240:808-819. PMID: 21360794
d. **Pierce ML**, Weston MD, Fritzsch B, Gabel HW, Ruvkun G, Soukup GA. (2008) MicroRNA-183 family conservation and ciliated neurosensory organ expression. Evol Dev. 10:106-113. PMID: 18184361

2. In the central nervous system, the oxytocin-vasopressin family are expressed in the social brain network and perturbations in expression are associated with psychopathologies including autism spectrum disorder, schizophrenia, anxiety, and depression. The oxytocin-vasopressin family is highly conserved in mammals, but recent discoveries have shown remarkable genetic variation in oxytocin ligands in New World Monkeys, with seven distinct ligand variants identified. To assess natural variation in oxytocin-vasopressin ligand-receptor pharmacological signatures, oxytocin receptor or vasopressin receptor 1a were stably transfected into CHO cells from four simian species: marmoset, titi monkey, macaque and human. We show that AVP, Leu8-OT and Pro8-OT display functionally distinct responses when activating the marmoset, titi monkey, macaque or human oxytocin receptor or vasopressin receptors. These distinct characteristics included peptide potency and efficacy, and G-protein subtype coupling. Currently, we are analyzing novel oxytocin analogs in primary neuronal cultures from a mouse model that expresses green fluorescent protein under the control of the oxytocin receptor as well as human-derived neuron-like SH-SY5Y cells that endogenously express human oxytocin receptor to better inform human oxytocin-mediated therapeutics.
    a. **Pierce ML,** French JA, Murray TF. (2020). Comparison of the pharmacologic profiles of arginine vasopressin and oxytocin analogs at marmoset, macaque, and human vasopressin 1a receptors. Biomed Pharmacother. Jun; 126: 110060 PMID: 32145592
    b. **Pierce ML**, French JA, Murray TM. (2020). Comparison of the pharmacologic profiles of arginine vasopressin and oxytocin analogs at marmoset, titi monkey, macaque, and human oxytocin receptors. Biomed Pharmacother. May; 125, 109832. PMID: 32018219.
    c. **Pierce ML,** Mehrotra S, Mustoe AM, French JA, Murray TM. (2019). A comparison of the ability of Leu^8- and Pro^8-oxytocin to regulate intracellular Ca^{2+} and Ca^{2+}-activated K^+ channels at human and marmoset oxytocin receptors. Mol Pharm. 2019 Apr;95(4):376-385. PMID: 30739093.

3. Natural products play important roles in ecology, biotechnology and biomedicine, with an estimated 60-70% of active compounds in clinical pharmaceutical formulations derived from or inspired by natural products. The marine environment is an extraordinarily rich source of species diversity, and marine organisms display vast chemical and biological diversity. Adaptation to their unique habitat contributes to marine organisms producing a wide variety of biologically active primary and secondary metabolites. Although major pharmaceutical companies have largely ceased exploring marine natural products following the development of large synthetic compound libraries, marine natural products continue to have a higher success rate than other sources of drug leads. Natural product scaffolds are generally not represented by synthetic compound libraries, providing novel chemical structures for new derivatives, mimetics, and semi-synthetic modifications to expand compound libraries. Currently, there are 19 FDA approved marine pharmaceuticals or derivatives and additional natural products in clinical trials. The neuroactive marine natural compound Ziconotide (Prialt), a potent conotoxin, was approved in 2004 for treatment of severe chronic pain, and Tetrodotoxin (Halneuron) is in phase III clinical trials. The goal of this research is to discover novel neuroactive compounds that may inform neuroscience drug development.
    a. Sequeira E, **Pierce ML**, Akasheh D, Sellers S, Gerwick WH, Baden DG, Murray TF. (2020). Epicortical Brevetoxin Treatment Promotes Neural Repair and Functional Recovery after Ischemic Stroke. Marine drugs. 21 July 2020 https://doi.org/10.3390/md18070374
    b. Li Y, Yu H, Zhang Y, Leao T, Glukhov E, **Pierce ML**, Zhang C, Kim H, Mao HH, Fang F, Cottrell GW, Murray TF, Gerwick L, Guan H, Gerwick WH. (2020). Pagoamide A, a cyclic depsipeptide isolated for a cultured marine chlorophyte, *Debesia sp.*, using MS/MS-based molecular networking. J Nat Prod. 2020 Jan 9. doi: 10.1021/acs.jnatprod.9b01019. PMID: 31916778
    c. Naman CB, Almaliti J, Armstrong L, Caro-Díaz EJ, **Pierce ML**, Glukhov E, Fenner A, Spadafora C, Debonsi HM, Dorrestein PC, Murray TF, Gerwick WH. (2017) Discovery and Synthesis of Caracolamide A, an Ion Channel Modulating Dichlorovinylidene Containing Phenethylamide from a Panamanian Marine Cyanobacterium cf. Symploca Species. J Nat Prod. Aug 7.

D. Peer-reviewed research publications (past 5 years)

1. Sequeira E, **Pierce ML**, Akasheh D, Sellers S, Gerwick WH, Baden DG, Murray TF. (2020). Epicortical Brevetoxin Treatment Promotes Neural Repair and Functional Recovery after Ischemic Stroke. Marine drugs. 21 July 2020 https://doi.org/10.3390/md18070374
2. **Pierce ML**, French JA, Murray TM. (2020). Comparison of the pharmacologic profiles of arginine vasopressin and oxytocin analogs at marmoset, macaque, and human vasopressin 1a receptors. Biomed Pharmacother. Biomed Pharmacother. 2020 Jun;126:110060.
3. **Pierce ML**, French JA, Murray TM. (2020). Comparison of the pharmacologic profiles of arginine vasopressin and oxytocin analogs at marmoset, titi monkey, macaque, and human oxytocin receptors. Biomed Pharmacother. 2020 May;125:109832.
4. Li Y, Yu H, Zhang Y, Leao T, Glukhov E, **Pierce ML**, Zhang C, Kim H, Mao HH, Fang F, Cottrell GW, Murray TF, Gerwick L, Guan H, Gerwick WH. (2020). Pagoamide A, a cyclic depsipeptide isolated for a cultured marine chlorophyte, Debesia sp., using MS/MS-based molecular networking. J Nat Prod. 2020 Jan 9. doi: 10.1021/acs.jnatprod.9b01019. PMID: 31916778
5. Banks SA, **Pierce ML**, Soukup GA. (2019). Sensational microRNAs: Neurosensory roles of the microRNA-183 family. Mol Neurobiol. 2019 Jul 29. doi: 10.1007/s12035-019-01717-3. Review. PMID: 31359323
6. **Pierce ML**, Mehrotra S, Mustoe AM, French JA, Murray TM. (2019). A comparison of the ability of Leu8- and Pro8-oxytocin to regulate intracellular Ca2+ and Ca2+-activated K+ channels at human and marmoset oxytocin receptors. Mol Pharm. 2019 Apr;95(4):376-385. PMID: 30739093.
7. Weston MD, Tarang S, **Pierce ML**, Pyakurel U, Rocha-Sanchez SM, McGee J, Walsh EJ, Soukup GA. (2018). A mouse model of miR-96, miR-182 and miR-183 misexpression implicates miRNAs in cochlear cell fate and homeostasis. Sci Rep. 2018 Feb 23;8(1):3569. doi: 10.1038/s41598-018-21811-1. PMID: 29476110
8. Naman CB, Almaliti J, Armstrong L, Caro-Díaz EJ, **Pierce ML**, Glukhov E, Fenner A, Spadafora C, Debonsi HM, Dorrestein PC, Murray TF, Gerwick WH. (2017). Discovery and Synthesis of Caracolamide A, an Ion Channel Modulating Dichlorovinylidene Containing Phenethylamide from a Panamanian Marine Cyanobacterium cf. Symploca Species. J Nat Prod. Aug 7.

E. Presentations/abstracts at national and international meetings (past 5 years) (student authors*, presenting author)

1. N. Vattem*, M. Scoles, A. Aziz*, A. Gore*, M. Gehr*, **M.L. Pierce.** "Effects of Oxytocin Analogs on Neurite Outgrowth and Cellular Signaling in Human SH-SY5Y Neuroblastoma Cell Line." Experimental Biology, Virtual Converence. 2021. Poster Presentation. Featured Poster for GPCR Colloquium.
2. **M.L Pierce** "Preclinical evaluation of novel OT-analogs for the potential treatment of social behavioral deficits." Drug Discovery and Development Annual Virtual Conference. 2021. Research Seminar. https://www.labroots.com/ms/virtual-event/drug-discovery-development-2021/speakers#marsha_pierce
3. **M.L. Pierce.** "Advocating early in your career as a neuroscientist". Society for Neuroscience. 2020. Moderator and Speaker. https://neuronline.sfn.org/advocacy/advocating-early-in-your-career-as-a-scientist
4. **M.L. Pierce.** "Effects of Arginine Vasopressin and Oxytocin on Neurite Outgrowth and Cellular Signaling in SH-SY5Y Human Neuroblastoma Cell Line." Experimental Biology, San Diego, CA. 2020. Abstract.
5. **M.L. Pierce**, J.A. French, T.F. Murray. "Comparison of pharmacological profiles of arginine vasopressin and oxytocin analogs at marmoset, macaque, and human oxytocin and vasopressin 1a receptors." Society for Neuroscience, Chicago, IL. 2019. Poster Presentation.
6. **M.L. Pierce**, J.A. French, T.F. Murray. "Impact of ligand and receptor variation in Anthropoidea vasopressin 1a receptor signaling". Society for Neuroscience, San Diego, CA. 2018. Poster Presentation.
7. **M.L. Pierce**, S. Merhotra, A.C. Mustoe, J.A. French, T.F. Murray. "Comparison of Leu8- and Pro8-oxytocin potency, efficacy and functional selectivity at the human and marmoset receptors." Society for Neuroscience, San Diego, CA. 2016. Poster Presentation.

Student Presentations (student authors*, presenting author)

1. S. Bhuvanagiri*, B. Panicker*, and **M.L. Pierce**. “Effects of oxytocin analogs on cellular signaling and neurite outgrowth in wild type and OXTR-EGFP murine primary hippocampal culture.” Chicago Society for Neuroscience. 2021. Virtual Poster Presentation.
2. N. Vattem*, A. Gore*, and **M.L. Pierce**. “Effect of oxytocin analogs on cellular signaling and neurite outgrowth in human SH-SY5Y neuroblastoma cell line.” Chicago Society for Neuroscience. 2021. Virtual Poster Presentation.
3. N. Vattem*, A. Gore*, and **M.L. Pierce**. “Effect of oxytocin analogs on cellular signaling and neurite outgrowth in human SH-SY5Y neuroblastoma cell line.” Midwestern University Kenneth A. Suarez University Research Day. 2021. Oral Presentation.
4. B. Panicker*, S. Bhuvanagiri*, and **M.L. Pierce.** “Effects of oxytocin analogs on cellular signaling and neurite outgrowth in wild type and OXTR-EGFP murine primary hippocampal culture.” Society for In Vitro Biology Annual Meeting 2021. Virtual Poster Presentation.
5. B. Panicker*, S. Bhuvanagiri*, and **M.L. Pierce.** “Effects of oxytocin analogs on cellular signaling and neurite outgrowth in wild type and OXTR-EGFP murine primary hippocampal culture.” Chicago Society for Neuroscience. 2021. Virtual Poster Presentation.

F. Grant Submission/funding track record (2019-present)

Title:	Effect of oxytocin analogs on pharmacological signaling and neuronal connectivity in murine primary neuronal cultures
Agency:	PhRMA Foundation
Amount:	$ 100,000
Submission Date:	September 1, 2019
Principal Investigator:	Marsha L. Pierce
Status:	Reviewed in November 2019. Not funded.

Title:	Effect of oxytocin analogs on social behaviors, pharmacological signaling, and neuronal connectivity in a mouse model of autism
Agency:	SFARI Foundation
Amount:	$ 300,000 (total); $ 267,550 (direct costs)
Submission Date:	September 13, 2019
Principal Investigator:	Marsha L. Pierce
Status:	Reviewed in October 2019. Not funded.

Title:	Effect of oxytocin analogs on learning and memory, pharmacological signaling, and neuronal connectivity in a mouse model of autism
Agency:	McKnight Foundation
Amount:	$ 225,000 (total); $ 225,000 (direct costs)
Submission Date:	January 1, 2020
Principal Investigator:	Marsha Pierce
Status:	Reviewed in April 2020. Not funded.

Title:	Effect of oxytocin analogs on pharmacological signaling, neurite outgrowth, and neuronal connectivity human-derived in vitro neuronal cell models
Agency:	NIH (R03)
Amount:	$ 150,000 (total); $ 100,000 (direct costs)
Submission Date:	February 16, 2020
Principal Investigator:	Marsha Pierce
Status:	Reviewed in April 2020. Not funded.

G. Students involved in the project

CURRENT STUDENTS

1. Nishita Vattem, CCOM, work study, March 2020—present
2. Supriya Bhuvanagri, CCOM, work study, March 2020—present

3. Bisini Panicker, CCOM, KAS 2020 Fellow, work study, March 2020—present
4. Marissa Gehr, CCOM, work study, June 2020—present
5. Ashley Gore, CCOM, volunteer, June 2020—present
6. Areej Aziz, CCOM, KAS 2021 Fellow, work study, March 2021-present
7. Angela Leschinsky, CCOM, work study, March 2021-present
8. Maryam Butts, CCOM, work study, March 2021-present
9. Rachel Han, CGS MABS, March-May 2021 [BISCD 0586]
10. Janki Patel, CCOM, M3 July 2021 Rotation

FORMER STUDENTS

1. Areej Aziz, CGS MABS, September-November 2019 volunteer, March-May 2020 [BISCD 0586]
2. Sharooq Elbagory, CGS MABS, September-November 2019 [BISCD 0584], March-May 2020 volunteer
3. Daniella Giraldo, CGS MABS, March-May 2020 [BISCD 0586]

H. Intramural Funding

Title:	High Throughput Screening of Marine Natural Products for Neuroactivity
Agency:	MWU One Health Initiative
Amount:	$ 10,000
Submission Date:	March 13, 2020
Principal Investigator:	Marsha Pierce
Co-Investigator:	William Gerwick
Co-Investigator:	Alex Mayer
Status:	**Funded in July 2020.**

Title:	Effect of oxytocin analogs on pharmacological signaling, neural maturation and neural connectivity in murine primary hippocampal cultures.
Agency:	MWU Intramural Funding
Amount:	$ 5,000
Submission Date:	May 15, 2020
Principal Investigator:	Marsha Pierce
Status:	**Funded in July 2020.**