BIOGRAPHICAL SKETCH

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NAME: Angela Henderson Redmond

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

POSITION TITLE: Assistant Professor of Research

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
Indiana University Bloomington (IU)	B.S.	1999-2003	Biology, with Distinction
Indiana University-Purdue University Indianapolis (IUPUI)	B.S.	2004-2006	Psychology
Indiana University-Purdue University Indianapolis (IUPUI)	M.S.	2006-2009	Psychobiology of Addictions
Indiana University-Purdue University Indianapolis (IUPUI)	Ph.D.	2009-2012	Psychobiology of Addictions
Pennsylvania State University (PSU) College of Medicine	Postdoctoral	2013-2019	Behavioral Neuropharmacology

A. Personal Statement

My career trajectory involve creating a strong translational research program focused on the neurobiological pathways that mediate sex differences in the response to analgesic drugs. I am seeking to fill a large translational gap in the clinical and preclinical literature examining sex-differences in the analgesic efficacy (or lack thereof) of both standard (opioid) and novel (i.e., cannabinoids) pharmacotherapies for managing chronic pain as well as the neurobiological mechanisms mediating these differences. Given that women comprise a greater proportion of the clinical population presenting with chronic pain, it is essential to understand how sex mediates differences both in how pain in processed, and more importantly, how it is managed. In particular, I am interested in using transgenic mouse models to better understand how manipulation of various receptors such as CB_1R and CB_2R, can differentially affect males and females and how these differences may be further modulated by alterations in sex hormones across the life cycle. Better understanding of how tolerance to cannabinoids is mediated as well as how alterations in sex hormones across age in both males and females can mediate analgesic outcomes to various types of pain (acute, inflammatory, and chronic, neuropathic pain), will hopefully enable the clinical development of more efficacious, diverse, non-opioid alternatives for the management of chronic pain.

B. Positions and Honors

Positions

2004-2006 Undergraduate Research Assistant, Psychobiology of Addictions Behavioral Science Laboratory of Drs. Nancy Badia-Elder and Robert Stewart, Department of Psychology, IUPUI, Indianapolis, IN

2005-2006 Undergraduate Teaching Assistant for Orientation to a Major in Psychology, Department of Psychology, IUPUI, Indianapolis, IN

2006-2012 Graduate Research Assistant, Psychobiology of Addiction/Addiction Neuroscience Program, IUPUI, Indianapolis, IN
2006-2007 Graduate Teaching Assistant for Lifespan Development, Department of Psychology, IUPUI, Indianapolis, IN
2007-2008 Graduate Instructor for Introduction to a Lab in Psychology, Department of Psychology, IUPUI, Indianapolis, IN
2013-2019 Postdoctoral Associate, Behavioral and Neuropharmacology Drug Addiction Laboratory of Dr. Daniel Morgan, Department of Anesthesiology & Perioperative Medicine, Penn State University College of Medicine, Hershey, PA
2019-2020 Research Associate, Departments of Anesthesiology & Perioperative Medicine and Pharmacology, Penn State University College of Medicine, Hershey, PA
2020-Present Assistant Professor of Research, Department of Biomedical Science, Marshall University, Huntington, WV

Honors

1999-2003 Indiana University Valedictorian Scholarship
2004-2006 School of Science Scholar, IUPUI
2006 GUZE Symposium on Alcoholism Travel Award
2007 Research Investment Fund (RIF) Fellowship, IUPUI
2008;2011-12 Research Society on Alcoholism Travel Award
2008-2012 NRSA Institutional Training Grant Pre-doctoral Appointment, IUPUI (AA007462)
2012 NIH National Graduate Student Research Conference Travel Award, Bethesda, MA
2015 Pennsylvania State Annual Postdoctoral Data and Dine First Place in Poster Competition
2016 ASPET Travel Award to Pharmacology in London, UK
2016-17 Penn State Dept. Anesthesiology & Perioperative Medicine Research Allocation Grant
2017; 2018 Gill Symposium Travel Award
2018 Division for Neuropharmacology Postdoctoral Scientist Award Finalist

Other Experience and Professional Affiliations

2000-2003 Alpha Chi Sigma Professional Chemistry Society
2002-2003 Phi Beta Kappa Honor Society
2006-2012 Research Society on Alcoholism
2008-Present Society for Neuroscience
2015 Progress in Neuro-Psychopharmacology & Biological Psychiatry ad hoc Reviewer
2016-Present American Society for Pharmacology and Experimental Therapeutics (ASPET)
2018 Drug and Alcohol Dependence Ad hoc Reviewer
2018 Alcoholism Clinical and Experimental Research Ad hoc Reviewer
2018-Present British Journal of Pharmacology ad hoc Reviewer
2018-Present International Cannabinoid Research Society (ICRS)
2018-Present Association for Psychological Science (APS)
2018-Present American Association for the Advancement of Science (AAAS)

Research Mentoring

Pennsylvania State University
Undergraduate:
Summer Interns: Tammy Lowe (Benedict College); Thomas Auen (Grinnell); Erin Ferguson (Boston University); Diana Castro Sepulveda (Penn State Harrisburg); Bradley Nolan (Lebanon Valley College)
Research Credit: Aaron Kline, Rachel Miller, Janelle Bowman, Virginia Gadalla-Saweirs; Sierra Rine; Veronika Oleksyuk
Graduate Students: Caitlin Nealon, Matthew Yuill, J. Dylan Van Kampen; Rebecca LaFleur; Mary Piscura; LaTaijah Crawford
Medical Students: Jeff Karduck, William Christie, Nathan DeTurk, Chandni Patel, David Hale, John Muller; Peter Milianta; Rahul Nachnani; Tim Helmuth

Medical Residents: Xibei Tian; Nicole Bashall

C. Contributions to Science
**Denote co-first author; [t] denotes corresponding author

"My Biography" at NCBI:
http://www.ncbi.nlm.nih.gov/sites/myncbi/angela.redmond.1/bibliography/49894480/public/?sort=date&direction=ascending

I. The role of neuropeptides in mediating alcohol-intake and associated behaviors in selected rats:

My early graduate career included examining the role of select neuropeptides, including neuropeptide S (NPS) and neuropeptide Y (NPY) on alcohol intake and alcohol-related behaviors in rats selectively bred to prefer (P) alcohol. I determined that the effects of NPS and NPY, when administered centrally, seem to selectively attenuate alcohol intake and have anxiolytic effects in P rats (but not in outbred Wistar or their non-preferring (NP) counterparts). I was also able to further elucidate the role of NPY in mitigating the alcohol deprivation effect in alcohol-dependent P and Wistar rats. Finally, I was able to verify that administration of NPY into the central nucleus of the amygdala (CeA), while able to mitigate alcohol consumption in both dependent and non-dependent P rats, only reduced alcohol intake and/or seeking "craving" behaviors in alcohol-dependent Wistar rats but not in non-dependent binge-drinking Long Evans rats while simultaneously validating the use of the sipper-tube model to promote binge-like drinking through assessment of blood alcohol levels (BALs).

Research Papers

Badia-Elder NE; **Henderson AN;** Bertholomey ML; Dodge NC; Stewart RB. (2008). The effects of neuropeptide S on ethanol drinking and other related behaviors in alcohol-preferring and –nonpreferring rats. Alcohol Clin Exp Res, 32:1380-1387. PMID:18564106

Gilpin NW; **Henderson AN**; Badia-Elder NE; Stewart RB. (2011). Effects of neuropeptide Y (NPY) and ethanol in arousal and anxiety-like behavior in alcohol-preferring (P) rats. Alcohol, 45:137-145. PMCID: PMC3021593

Bertholomey ML; **Henderson AN**; Badia-Elder NE; Stewart RS. (2011). Effects of neuropeptide Y (NPY) – induced reductions in alcohol intake during continuous access and following alcohol deprivation are not altered by restraint stress in alcohol-preferring (P) rats. Pharmaco Biochem Behav, 97:453-461. PMCID: PMC3006030

Henderson AN; Czachowski CL. (2012). Neuropeptide Y (NPY) in the central nucleus of the amygdala (CeA) does not affect ethanol-reinforced responding in binge-drinking, nondependent rats. Pharmaco Biochem Behav, 101:8-13. PMCID: PMC3272140

II. The role of the endogenous opioid system in mediating alcohol and morphine reward:

The latter portion of my graduate career and early postdoctoral career saw me delve into understanding how the endogenous opioid system mediates alcohol reward and craving. This was done first through my dissertation where I used select opioid agonists and antagonist to assess the contribution of each opioid receptor subtype on alcohol intake and "seeking" behaviors using the sipper-tube model. I subsequently determined that blocking the delta opioid receptor selectively attenuated alcohol intake in P rats only while activation of the kappa opioid receptor decreased both alcohol seeking and intake in P and non-selected rats alike. As the A118G polymorphism has been indicated in mediating responsiveness to naltrexone clinically in alcoholics, I decided to examine how the use of mice genetically altered to express either the wild-type (A) or mutant (G) variant of the A118G polymorphism of the mu opioid receptor responding to morphine and alcohol.
Interestingly, I found while mutants of both sexes drank more alcohol than their wild-type counterparts, female mutants were significantly less affected by the sedative/hypnotic effects of alcohol while male mutants showed a greater response to the rewarding effects of alcohol than their respective wild-type counterparts.

Research Papers

Henderson-Redmond A; Czachowski C. (2014). Effects of systemic opioid receptor ligands on ethanol- and sucrose seeking and drinking in alcohol-preferring (P) and Long Evans rats. Psychopharmacology (Berl), 231:4309-4321. PMCID: PMC4209193

Henderson-Redmond AN; Yuill MB; Lowe TE; Kline AM; Zee ML; Guindon J; Morgan DJ. (2016). Morphine-induced antinociception and reward in "humanized" mice expressing the mu opioid receptor A118G polymorphism. Brain Res Bull, 123:5-12. PMCID: PMC4848164

Henderson-Redmond AN[t]; Lowe TC; Tian X; Morgan DJ. (2018). Increased ethanol drinking in "humanized" mice expressing the mu opioid receptor A118G polymorphism are mediated through sex-specific mechanisms. Brain Res Bull, 138: 12-19. PMCID: PMC5796878

Invited Talk

Increased ethanol drinking in "humanized" mice expressing the mu-opioid receptor A118G polymorphism are mediated through sex-specific mechanisms. Presented at the 2nd Annual Pennsylvania State University Addiction Symposium, Pennsylvania State University College of Medicine, Hershey, PA, April 4, 2016

III. Characterization of mice expressing a desensitization-resistant form of the CB_1 receptor:

Following up on *in vitro* work showing that blocking desensitization of the cannabinoid type-1 receptor (CB1R) prolonged CB1R receptor activation, a CB1R desensitization-resistant "mutant" mouse model (the S426A/S430A mouse) was created to assess whether blocking desensitization of CB1R *in vivo* could likewise decrease the rate of tolerance development to CB1R agonists. Through characterization of this mouse, we determined that the S426A/S430A mutation did not produce either obese or diabetic mice, but did modestly enhance alcohol (but not morphine or cocaine) preference and reward. We showed that the S426A/S430A mutation resulted in a considerable delay in the development of tolerance to the partial CB1R agonist delta-9-tetrahydrocannabinol (Δ^9-THC), and to the full CB1R agonists CP55,940 and WIN55,212-2 in male mice. Further, I showed that pretreatment with the selective c-Jun N-terminal kinase (JNK) inhibitor SP600125 (SP6) further delayed analgesic tolerance development across multiple pain models (acute thermal, acute inflammatory, and a chronic pain model of neuropathy). Even more interesting, I found that this effect was selective for Δ^9-THC, as pretreatment with SP6 had no effect on altering tolerance development to WIN55,212-2 and, conversely, accelerated tolerance development in mice treated CP55,940. These findings demonstrate functional selectivity for the CB1R and could have important implications clinically in how we treat pain with the increasing legalization of medicinal marijuana.

Research Papers

Marcus DJ; Zee ML; Davis BJ; Haskins CP; Andrews MJ; Amin R; **Henderson-Redmond AN**; Mackie K; Czyzyk TA; Morgan DJ (2016). Mice expressing a "hyper-sensitive" form of the cannabinoid receptor 1 (CB_1) are neither obese nor diabetic. PLoS One, 11: e0160462. doi: 10.1371/journal.pone.0160462 PMCID: PMC4976987

Marcus DJ**; **Henderson-Redmond AN****;** Gonek M; Zee ML; Farnsworth JC; Amin RA; Andrews MJ; Davis B; Mackie K; Morgan DJ. (2017). Mice expressing a "hyper-sensitive" form of the CB_1 cannabinoid receptor (CB_1) show greater alcohol preference and consumption. PLoS ONE. doi: 10.1371/journal.pone.0174826. PMCID: PMC5398885

Nealon CM; **Henderson-Redmond AN;** Hale DE; Morgan DJ. (2019). Tolerance to WIN55,212-2, but not CP55,940, is profoundly delayed in desensitization-resistant S426A/S430A mice. Neuropharmacology, 148: 151-159. doi:10.1016/j.neuropharm.2018.12.016 PMID:30629988

Henderson-Redmond AN;** Nealon CM**; Davis BJ**; Yuill MB; Sepulveda DE; Blanton HL; Piscura MK; Zee ML; Haskins CP; Marcus DJ; Mackie K; Guindon J; Morgan DJ. (2020) c-Jun N terminal kinase signaling pathways mediate cannabinoid tolerance in an agonist specific manner. Neuropharmacology, 164: 107847. doi: 10.1016/j.neuropharm.2019.107847

IV. Sex differences mediated by the CB_1R

Most recently, I have become interested in how sex and agonist-specific differences mediate differences in sensitivity and analgesic responses across a variety of pain modalities. I have found that females are less sensitive to the acute antinociceptive effects of CB_1R agonists (including CP55,940, Δ^9-THC, and WIN55,212-2) than their male counterparts. Of particular note, female mice appear to develop tolerance faster to the antinociceptive effects of Δ^9-THC but do not differ from males in the rate of antinociceptive tolerance to CP55,940

in an acute thermal pain model. These data are currently serving as the preliminary data for the present grant proposal where I hope to continue to study these effects and to better understand the role of sex differences in neuropathic pain models and the mechanisms mediating our observed sex-differences, which is increasingly relevant given the recent legalization of medical marijuana as an alternative to pain management in an effort to combat the opioid crisis. Finally, we showed that blocking desensitization of CB_1R resulted in greater changes in affect in female (but not male) mice following the induction of chronic pain. These findings serve as preliminary data for a separate proposal I am developing to better understand how sex-differences in affect can alter pain sensitivity and analgesic responses and tolerance development of drugs used to manage chronic pain.

Research Papers

LaFleur RA; Wilson RP; Morgan DJ; **Henderson-Redmond AN[t].** (2018). Sex differences in antinociceptive response to delta-9-tetrahydrocannabinol and CP55,940 in the mouse formalin test. Neuroreport, 29:447-452. PMCID: PMC6112616.

Henderson-Redmond AN[t]; Sepulveda DE; Ferguson EL; Kline AM; Piscura M; Rine SA; Oleksyuk V; Morgan DJ. Sex-specific mechanisms of acute antinociceptive and anti-inflammatory tolerance to Δ^9-THC and CP55,940 in desensitization-resistant S426A/S430A and wild-type mice. *In Preparation to be submitted August 2020*

Invited Talks

Sex and agonist specific differences in cannabinoid tolerance in desensitization-resistant S426A/S430A mice. Presented at the Winter Conference of Brain Research Conference, Big Sky Lodge, Big Sky, MO, January 30, 2017

Sex Differences in antinociceptive tolerance development to Δ^9-THC and CP55,940 in wild-type and desensitization-resistant S426A/S430A mice. Presented at Experimental Biology as a Finalist in the Division for Neuropharmacology Postdoctoral Scientist Award, San Diego, CA, April 23, 2018

D. Additional Information: Research Support and/or Scholastic Performance

Research Support/Funding Mechanisms

Completed Research Mechanisms

Resource Allocation Panel Redmond (PI) 06/01/16-05/31/17
Department of Anesthesiology & Perioperative Medicine, Penn State College of Medicine
Sex-Specific Mechanisms Mediate Increased Drinking in A118G Mice
The goal of this study is to determine the mechanisms mediating increased ethanol consumption in male and female mice expressing the humanized mutant A118G variant (GG) of the OPRM1 gene
Role (PI)

T32 AA007462 McBride (PI) 05/24/08-05/23/12
NIH/NIAAA
Ruth L. Kirschstein National Research Service Award Training Grant of Genetic Aspects of Alcoholism.
Institutional Training Program at Indiana University-Purdue University Indianapolis
The goal of this study was to understand the genetic differences that mediate ethanol intake and reward
Role (Trainee)