BIOGRAPHICAL SKETCH

NAME: Angela Henderson Redmond

eRA COMMONS USER NAME: ANHENDER

POSITION TITLE: Assistant Professor of Research

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Indiana University, Bloomington (IU)	B.S.	05/2003	Biology
Indiana University-Purdue University Indianapolis (IUPUI)	B.S.	05/2006	Psychology
Indiana University-Purdue University Indianapolis (IUPUI)	M.S.	08/2009	Psychobiology of Addictions/ Addiction Neuroscience
Indiana University-Purdue University Indianapolis (IUPUI)	Ph.D.	05/2012	Psychobiology of Addictions/ Addiction Neuroscience
Pennsylvania State University (PSU) College of Medicine, Hershey	Postdoctoral	05/2019	Behavioral Neuropharmacology

A. Personal Statement

My career trajectory involves creating a strong translational research program focused on identifying the neurobiological pathways that mediate sex-differences both in neuropathic pain development and in sensitivity and tolerance development to select pharmacotherapies used in the management of chronic pain. Working closely with clinicians, I am seeking to fill a large gap in the clinical and preclinical literature regarding both sex-differences in analgesic efficacy (or lack thereof) to standard (opioid) and novel pharmacotherapies (i.e., cannabinoids, including CBD) for the management of chronic pain and the neurobiological mechanisms mediating these differences. Given the current opioid crisis and the increasing legalization and recognition of cannabis for its analgesic properties, it is my goal to utilize various mouse models of chronic pain to assess the clinical potential of cannabis and cannabis-derived compounds, including delta-9-tetrahydrocannabinol (Δ^9-THC) and especially cannabidiol (CBD) for managing chronic pain. My most recently published data assessing the analgesic potential of various cannabinoids has demonstrated that female wild-type mice are much less sensitive to the antinociceptive and analgesic effects of Δ^9-THC both in an acute model of thermal pain (Henderson-Redmond et al., 2022) and in a more clinically relevant model of chemotherapy-evoked neuropathic pain (Henderson-Redmond, 2021). Likewise, females were less sensitive to the anti-inflammatory effects of CBD in the formalin model of inflammatory pain (Barnes et al., 2024). As more women than men suffer from chronic pain conditions, it is essential to understand what sex differences may mediate these differences in effect, and whether these effects are species or strain specific (Lulek et al., 2023). It is also necessary to identify whether the observed differences in analgesic response are due to sex-differences in hormone levels, gene expression, cannabinoid receptor coupling or density, some combination of these factors, or some other mechanisms entirely. Because pain development is sexually dimorphic and often is concomitant with negative affect (more prominent in females) and substance abuse disorders (more prominent in men), recent research has also examined whether there are sex differences in vulnerability to affect of alcohol use following traumatic brain injury with TBI inducing increased alcohol intake in a sex-specific manner (Xu et al., 2025). More recently, I have begun looking at the non-psychoactive component of cannabis, cannabidiol (CBD), to better understand how CBD can be utilized both alone and as an adjuvant to combat chronic pain in clinically relevant pain models. My preliminary findings underscore the effectiveness of CBD in chronic (but not acute) pain states and the lack of psychoactive effects indicates limited abuse potential. Further, I have begun to explore how use of CBD may prevent the development of neuropathic pain, and given the sexual dimorphism in pain development, whether there are sex differences in the effectiveness of CBD and its mechanisms of action (via inflammation). Ultimately,

I would like to incorporate the findings from my preclinical studies to examine the clinical efficacy of CBD particularly in patient populations that have experienced various forms of chronic pain and those that have developed concomitant substance abuse disorders as a form of "self-medication," to help identify better ways to treat pain and prevent substance use disorders from developing by limiting the formation of chronic pain or finding better alternatives to manage pain from the onset.

Awarded/Ongoing Funding:

WV-CTSI Henderson-Redmond (PI) 10/11/24-10/10/25
West Virginia Clinical and Translational Science Institute Rapid Response Competitive Research Grant ($30K/year). Title: Cannabidiol (CBD) decreases pain sensitivity and morphine usage in neuropathic pain. The aim of this competitive grant is to acquire preliminary data on the use of CBD to mitigate pain and the effect on morphine efficacy in a chemotherapy-evoked model of neuropathic pain.

Past Support

Yale/NIDA Neuroproteomics Center Henderson-Redmond (PI) 06/1/2023-5/31/2024
Title: "Understanding biased CB_1R signaling through phospho-proteomics." The aim of this competitive pilot project is to utilize HA-tagged CB1 cells treated with different CB1 agonists (including THC and CP55,940) at time points that stimulate either desensitization or internalization and utilize phospho-proteomics to assess differentially activated proteins.

WV-INBRE Henderson-Redmond (PI) 08/01/2022-07/31/2024
West Virginia IDeA Network of Biomedical Excellence Center for Natural Products Competitive Research Grant. This project investigates the role of decursinol (a natural extract of the Korean Angelica plant), in mitigating chemotherapy-evoked neuropathic pain and as a potential adjuvant to morphine in mice.

Research Allocation Grant Henderson-Redmond (PI) 05/1/2016-04/30/2017
Department of Anesthesiology & Perioperative Medicine Research Allocation Panel Starter Grant.
Title: "Sex-specific mechanisms mediate increased drinking in A118G mice." This study assessed sex differences in genetically modified mice that expressed either the human version of the 118GG or 118AA allele on binge ethanol drinking, naltrexone intervention, and alcohol related preferences and behaviors.

B. Positions and Honors

Positions

2021-Present	Instructor for BMR650 Drugs and Behavior, Department of Biomedical Sciences, Marshall University, Huntington, WV
2020-Present	Assistant Professor of Research, Department of Biomedical Science, Marshall University, Huntington, WV
2019-2020	Research Associate, Departments of Anesthesiology & Perioperative Medicine and Pharmacology, Penn State University College of Medicine, Hershey, PA
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
2007-2008	Graduate Instructor for Introduction to a Lab in Psychology, Department of Psychology, IUPUI, Indianapolis, IN
2006-2007	Graduate Teaching Assistant for Lifespan Development, Department of Psychology, IUPUI, Indianapolis, IN
2006-2012	Graduate Research Assistant, Psychobiology of Addiction/Addiction Neuroscience Program, IUPUI, Indianapolis, IN
2005-2006	Undergraduate Teaching Assistant for Orientation to a Major in Psychology, Department of Psychology, IUPUI, Indianapolis, IN
2004-2006	Undergraduate Research Assistant, Psychobiology of Addictions Behavioral Science Lab of Drs. Nancy Badia-Elder and Robert Stewart, Department of Psychology, IUPUI, Indianapolis, IN

Honors

2018	Division for Neuropharmacology Postdoctoral Scientist Award Finalist
2017; 2018	Gill Symposium Travel Award
2016-17	Penn State Dept. Anesthesiology & Perioperative Medicine Research Allocation Grant
2016	ASPET Travel Award to Pharmacology in London, UK
2015	Pennsylvania State Annual Postdoctoral Data and Dine First Place in Poster Competition

2012 NIH National Graduate Student Research Conference Travel Award, Bethesda, MA
2008-2012 NRSA Institutional Training Grant Pre-doctoral Appointment, IUPUI (AA007462)
2008;2011-12 Research Society on Alcoholism Travel Award
2007 Research Investment Fund (RIF) Fellowship, IUPUI
2006 GUZE Symposium on Alcoholism Travel Award
2004-2006 School of Science Scholar, IUPUI
1999-2003 Indiana University Valedictorian Scholarship

Other Experience and Professional Affiliations

2024-Present Neuropharmacology ad hoc reviewer
2023-Present Pharmacological Reviews ad hoc reviewer
2022 ASPET Division of Neuropharmacology Judge for Annual Poster Competition
2022-Present Frontiers in Neuroscience Ad hoc Reviewer
2021-Present WV-CTSI 2021 Symposium on Substance Abuse Research Program Committee Member
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)
2018 Drug and Alcohol Dependence Ad hoc Reviewer
2018 Alcoholism Clinical and Experimental Research Ad hoc Reviewer
2016-Present American Society for Pharmacology and Experimental Therapeutics (ASPET)
2015 Progress in Neuro-Psychopharmacology & Biological Psychiatry ad hoc Reviewer
2008-Present Society for Neuroscience
2006-2012 Research Society on Alcoholism
2002-2003 Phi Beta Kappa Honor Society
2000-2003 Alpha Chi Sigma Professional Chemistry Society

C. Contributions to Science

Complete list of Published Work in "My Biography" at NCBI:
https://www.ncbi.nlm.nih.gov/sites/myncbi/angela.redmond.1/bibliography/49894480/public
**Denote co-first or co-senior author; [t] denotes corresponding author

I. The role of neuropeptides in mediating alcohol-intake and associated affective 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 affective 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. doi: 10.1111/j.1530-0277.2008.00713.x 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. doi: 10.1016/j.alcohol.2010.08.019 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. doi: 10.1016/j.pbb.2010.10.002 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. doi: 10.1016/j.pbb.2011.11.008 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. doi: 10.1007/s00213-014-3571-9 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. doi: 10.1016/j.brainresbull.2015.10.007 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. doi: 10.1016/j.brainresbull.2017.07.017 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 modestly enhanced alcohol (but not morphine or cocaine) preference and reward. We showed that the S426A/S430A mutation delayed 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. 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) but 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**; **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 PMCID: PMC6535342

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 PMID: 31758947

Piscura MK; Sepulveda D; Maulik, M., Guindon G; **Henderson-Redmond A**;** Morgan D**. (2023). S426A/S430A phosphorylation of CB1R accounts for the effects of beta-arrestin 2-mediated desensitization on cannabinoid response and tolerance. JPET, 385: 17-34. https://doi.org/10.1124/jpet.122.001367

IV. Sex differences in cannabinoid-mediated analgesia

Most recently, I have become interested in how sex differences mediate differences in sensitivity and analgesic responses across a variety of pain modalities. I have found that female wild-type B6 mice are less sensitive to the acute antinociceptive effects of cannabinoid agonists (including CP55,940, Δ^9-THC, and WIN55,212-2) than their male counterparts. Of 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. Likewise, I have found that female wild-type mice show only a partial reversal of allodynia at doses of Δ^9-THC that otherwise fully reversed allodynia in male wild-type mice in a cisplatin-evoked model of neuropathic pain. At present, these data along with alterations in select cytokine levels, the influence of sex hormones, and the role of the estrus cycle in mediating chronic neuropathic pain will serve as preliminary data for a separate grant proposal currently in development. A better understanding of how sex differences can mediate both pain and analgesic responses in various models of chronic pain is increasingly relevant given the recent legalization of medical marijuana as an alternative to pain management to combat the opioid crisis. Interestingly, while tolerance seems to occur faster clinically and among different mouse lines, sex-difference in cannabinoid-analgesia may be line dependent in mice and we show that this directionality may correlate with CB1 gene expression in the PAG. Finally, we showed the altering desensitization through the mutation of serines 426 and 430 in the distal tail of the CB1 receptor increased Δ^9-THC- and CP55,940-mediated antinociception in a model of acute, thermal pain but did not affect sensitivity to Δ^9-THC in a model of neuropathic pain, likely highlighting the greater involvement of CB2 receptors in chronic pain models.

Research Papers

Henderson-Redmond AN^t; Crawford LC; Sepulveda DE; Hale DE; Lesperance JJ; Morgan DJ. (2021). Sex differences in tolerance to delta-9-tetrahydrocannabinol (Δ^9-THC) in mice with cisplatin-evoked chronic neuropathic pain. Frontiers in Molecular Biosciences: Molecular Diagnostics and Therapeutics. doi:10.3389/fmolb.2021.684115. PMCID: PMC8267820

Henderson-Redmond AN^t; Sepulveda DE; Ferguson EL; Kline AM; Piscura MK; Morgan DJ. (2022). Sex-specific mechanisms of tolerance for the cannabinoid agonists CP55,940 and delta-9-tetrahydrocannabinol (Δ^9-THC). Psychopharmacology (Berl). 239:1289-1309. Doi: 10.1007/s00213-021-05886-9. PMID: 34165606: PMCID: 8702575

Lulek CF; Maulik M; Mitra S; Guindon J; Morgan DJ; **Henderson-Redmond AN^t**. (2023). Sex differences in acute delta-9-tetrahydrocannabinol (Δ^9-THC) response and tolerance as a function of mouse strain. Psychopharmacology, 240:1987-2003. doi.org/10.1007/s00213-023-06421-8. PMID:37516707: PMCID:PMC10471687

Barnes RC; Banjara S; McHann MC; Almodovar S; **Henderson-Redmond AN;** Morgan DJ; Castro-Piedras I; Guindon J. (2024). Assessing dose-and sex-dependent antinociceptive effects of cannabidiol and amitriptyline, alone and in combination, and in exploring mechanisms of action involving serotonin 1A receptors. JPET, 388:655-669. doi.org/10.1124/jpet.123.001855