



Grant Proposal Development

Scott Edwards, PhD

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Dept of Physiology Vice Chair for Training and Mentoring

LSU Health
NEW ORLEANS

School of Medicine Research Café Schedule

Dates	Topic	Facilitator
September 9	Intramural Funding Opportunities and Strategies	Peter Winsauer, PhD
October 14	Grant Proposal Development	Scott Edwards, PhD
November 11	Writing Specific Aims	Nick Gilpin, PhD
December 9	Writing Research Strategy Sections	David Welsh, MD
January 13	Preparing NIH Biosketches, Budgets, and Budget Justifications	Peter Winsauer, PhD & Carly Pigg, CRA, CPRA, CFRA
February 10	Preparing for IBC Applications	Arnold Zea, PhD
March 10	Preparing IACUC Applications	Charles Nichols, PhD
April 14	Preparing and Submitting IRB Applications	Jessica Rivera, MD, PhD
May 12	Basics of Submitting Extramural Fellowship Applications	Scott Edwards, PhD, Nick Harris, Eden Gallegos
June 9	Basics of Submitting Extramural Career Development Awards	Nick Gilpin, PhD, Sydney Vita, PhD, Amanda Pahng, PhD
July 14	Preparing Ancillary Documents	Liz Simon, PhD

Learning Objectives



- Distinguish between different NIH activity codes and NIH funding mechanisms
- Recognize and describe the major components of a typical NIH grant proposal
- Navigate the NIH grant submission process and the necessary coordination with institutional offices



Why Should You Think About Grants Now?



- Grants are mechanism by which to prove that you can envision a major research trajectory, with the requisite balance of independence and collaborative skill.
- Grantsmanship can take years to develop, but once the skill is developed, it is highly transferrable and valuable to current and future employers.
- It is never too early or too late to start! Also, you're surrounded by investigators and collaborators who could use help with grant writing.
- Be prepared for future opportunities from other sources – you might get looped into a research project or study as a valuable co-investigator and things move quickly.

Extramural Funding Opportunities



National Institutes
of Health



hhmi



NIH Extramural Research Funding

- The NIH's mission is to fund the best scientific projects to improve public health (sometimes the rich get richer).
- Approximately 80% of NIH budget is for extramural research.
- The merit of each application is reviewed by NIH's peer review system (including you and me).



Major NIH Funding Mechanisms

- Grants = investigators are responsible for developing the concepts, methods, and approach for a research project.
 - Solicited = NIH institute seeks applications in a specific area
 - Unsolicited = Proposal initiated by the principal investigator
- Contracts = the NIH institute is responsible for establishing the detailed requirements.
 - Principal Investigators will submit a competitive bid offer

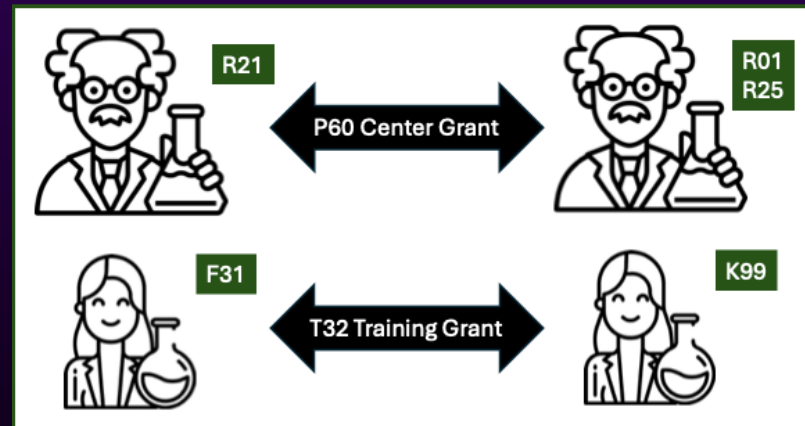
National Institutes of Health (NIH) Institutes & Centers

- 27 institutes and centers (congressional limit!)
- Most are specific to a disease of national interest:
 - National Cancer Institute (NCI)
 - National Heart, Lung, and Blood Institute (NHLBI)
 - National Institute on Drug Abuse (NIDA)
 - National Institute on Alcohol Abuse and Alcoholism (NIAAA)
 - National Institute on Mental Health (NIMH)
 - National Institute of General Medical Sciences (NIGMS)

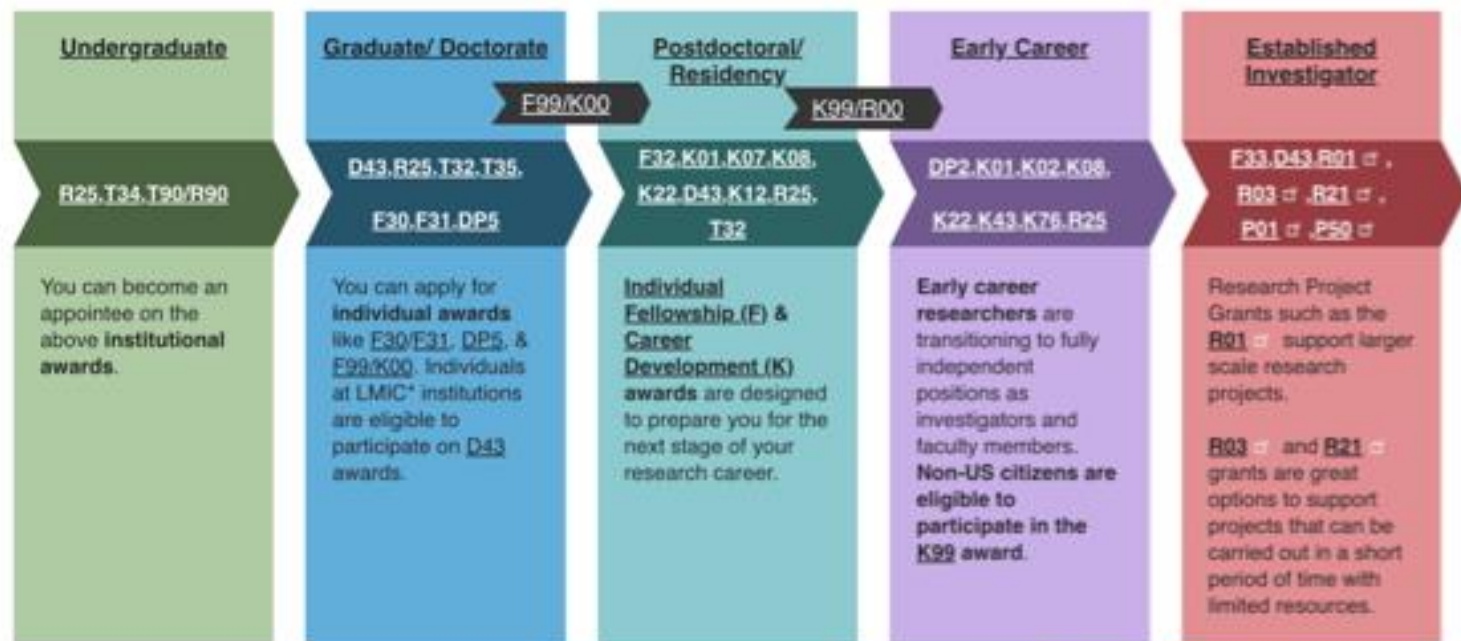


NIH Extramural Activity Codes

- Research Projects (R series)
- Career Development (K series)
- Fellowship Awards (F series)
- Training Programs (T series)
- Projects & Centers (P series)



NIH Funding Programs by Career Stage



\$50K/year *** LOAN REPAYMENT PROGRAMS *** \$50K/year

SUPPLEMENTS TO ACTIVE AWARDS TO ENHANCE DIVERSITY, PROMOTE RE-ENTRY, AND MORE

Key

F = Fellowship
K = Career Development

R = Research
T = Training

P = Program Project/Center

Fellowship Award Programs

Provide stipend, tuition, and small institutional allowance



- F₃₀ – Predoctoral fellowship for MD/PhD students
- F₃₁ – Predoctoral fellowship for PhD students
- F₃₂ – Postdoctoral fellowship
- F₉₉/K₀₀ – Transition from predoctoral to postdoctoral training

Basic science and clinical faculty provide essential mentoring!

Career Development Awards (PhD Focus)

K01 Criteria (Mentored Career Development Award)

- **Eligibility Requirements:** Doctoral degree, faculty or equivalent position, U.S. citizen or permanent resident
- **Award Duration:** Three to five years
- **Due Dates:** Feb. 12/March 12, June 12/July 12, Oct. 12/Nov. 12
- **Budget:** Up to \$75,000 salary and \$20,000 research support



Often (not always) stay local

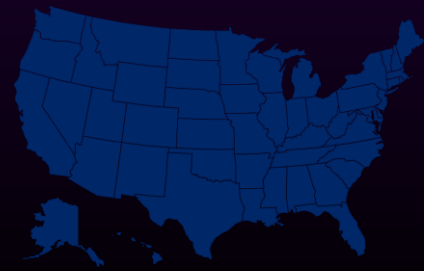


K99 Criteria (Pathway to Independence Award)

- **Eligibility Requirements:** Doctoral degree, up to four years postdoctoral experience
- **Award Duration:** Two years postdoctoral
- **Due Dates:** Feb. 12, June 12, Oct. 12
- **Budget:** Up to \$75,000 salary and \$25,000 research support



Often (not always) leave



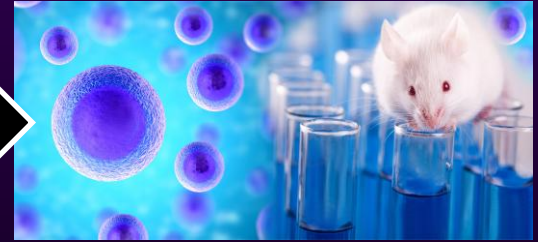
Career Development Awards (Post-MD, Residency)

K08 at a Glance

- **Eligibility Requirements:** Clinical doctoral degree, U.S. citizen or permanent resident
- **Award Duration:** Three to five years
- **Due Dates:** Feb. 12/March 12, June 12/July 12, Oct. 12/Nov. 12
- **Budget:** Up to \$100,000 salary and \$25,000 research support



Preclinical or Basic Science



K23 at a Glance

- **Eligibility Requirements:** Clinical doctoral degree, U.S. citizen or permanent resident
- **Award Duration:** Three to five years
- **Due Dates:** Feb. 12/March 12, June 12/July 12, Oct. 12/Nov. 12
- **Budget:** Up to \$100,000 salary and \$25,000 research support



Clinical or Patient-Centered



Research Project Grants & Budgets

- R01 – Discrete, specified major projects
 - \$1.25M over five years (can be more)
- R03 - Preliminary, short-term projects
 - \$50K (also consider internal SOM grant)
- R21 – Exploratory, developmental grants
 - \$375K over two years
- R25 – Education projects



Sustainable Program for Health Care Professionals to Develop Skills
and Confidence Related to Alcohol Use Screening and Treatment

LSU Health
NEW ORLEANS

New Investigators (NI) and Early-Stage Investigators (ESI)



- NI = Has not previously received a significant award from NIH
 - Perhaps previous funding from NSF or other source
- ESI = Within ten years of terminal degree or post-grad training
 - Terminal degree typically PhD or MD, & postdoc training
- Special privileged paylines for Ro1s:
 - Edwards was ESI in 2019, & NIAAA paylines were 18% vs. 28% ESI



Research Program Projects and Centers

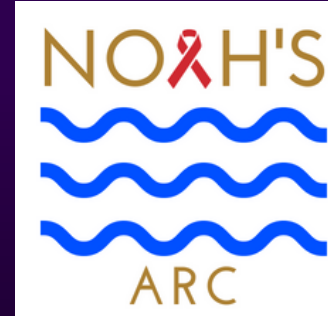
- P01 – Research Program Project
- P50 – Specialized Center Grant (More Integrative)
- P60 – Comprehensive Center Grant (Includes Outreach)
- To support multipurpose units designed to bring together into a common focus divergent but related facilities within a given research community



LSU HEALTH SCIENCES CENTER
**COMPREHENSIVE ALCOHOL-
HIV/AIDS RESEARCH CENTER**

Biomedical Consequences of Alcohol & HIV

LSU HEALTH SCIENCES CENTER COMPREHENSIVE ALCOHOL- HIV/AIDS RESEARCH CENTER

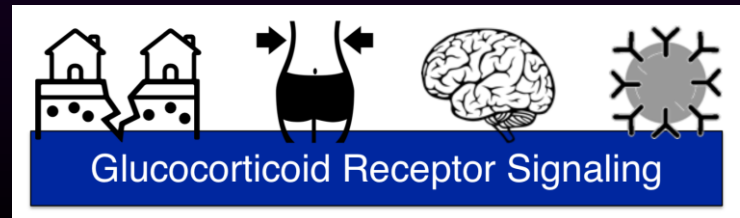


RC1: Environmental Stressors Underlying Anxiety & Depression:
Factors in Alcohol Associated Comorbidities in PWH

RC2: Alcohol and Metabolic Dysregulation in PWH:
Mechanisms Underlying Risk for Comorbidities

RC3: Pain, Negative Affect, and Cognitive Dysfunction at the
Intersection of HIV and AUD Risk

RC4: Alcohol, Immunosenesence, & Senodynamics in PWH



Small Business Grants



- R_{41}/R_{42} = Small Business Technology Transfer (STTR)
 - Supports cooperative research projects between small business and research institutions. To establish merit and feasibility ideas with potential for commercialization.
- R_{43}/R_{44} = Small Business Innovation Research (SBIR)
 - Supports projects to establish technical merit and feasibility that lead to commercial products and services.

Formal NIH Training Programs

- T₃₂ – Fund academic institution for training predoctoral and postdoctoral candidates.
 - T₃₂ Biomedical Alcohol Research Training Program
- T₃₅ – Provide short-term research training.
 - Summer student research experiences
 - T₃₅ Medical Student Alcohol Research Internship

Basic science and clinical faculty provide essential mentoring!



NIH/NIAAA T₃₅ Medical Student
Alcohol Research Internship
Summer 2025 Cohort

Major Components of an NIH Proposal



NIH Biographical Sketch

- Somewhat of a resumé and CV combo.
- For collaborative grants all associated personnel will submit an NIH Biosketch describing their role in the proposal.
 - Principle Investigator (You)
 - Sponsor & Co-Sponsors
 - Collaborators & Consultants
- You will submit this anytime you are part of a formal NIH grant proposal in your career.
 - Make one now!
 - And then customize for each use.

Research Café Date: Jan 13, 2026

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Lee, Sumin (Stephanie)

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

POSITION TITLE: Graduate Research Assistant

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)	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Emory University, Atlanta, GA	BS	08/2017	12/2020	Neuroscience and Behavioral Biology
Louisiana State University Health Sciences Center, New Orleans, LA	MD/PhD	07/2021	05/2028 (Expected)	Medicine, Physiology

A. Personal Statement

As an aspiring physician-scientist, my aim in pursuing training at Louisiana State University Health Sciences Center (LSUHSC) is to cultivate skills required to establish a successful career in translational research. From a young age, I knew medicine would play a central role in my future, but it was my experience as a clinical research coordinator at the Emory Behavioral Immunology Program that ignited a deep passion for research in my professional journey. Working on a project investigating the responsiveness to bupropion in patients with major depression in the context of inflammation exposed me to the profound impact of translating molecular neurobiology into clinical practice to enhance patient outcomes.

Seeking to further align myself with my career objectives, I embarked on a T35 research fellowship, sponsored by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), during the summer after my first year of medical school. This immersive experience shed light on the significant knowledge gap concerning the mechanisms underlying the anti-nociceptive effects of alcohol, particularly in relation to chronic pain and its contribution to alcohol use disorder (AUD). My investigations, centered on exploring sex differences in pain perception and modulation after acute alcohol use in both pre-clinical and clinical models, deepened my fascination with alcohol research and the profound possibilities of translational studies. These experiences steered me towards the decision to pursue a combined MD/PhD program, rather than solely an MD degree.

Currently, my specific focus centers around neural modulations in the central endocannabinoid system following alcohol use and the consequential impact on pain experience and relapse of AUD. In the pursuit of this passion, I am eager to undergo training at LSUHSC, particularly under the mentorship of Dr. Scott Edwards. Dr. Edwards' expertise in alcohol and neuroscience research is poised to play a crucial role in the success of my future projects. I am also impressed by Dr. Edwards' commitment to nurturing my growth as a physician-scientist that extends beyond the lab through the development of teaching skills and engagement in community outreach and service, which truly resonates with my own aspirations. The Ruth L. Kirschstein Institutional National Research Service Award (NRSA) training fellowship, combined with my Comprehensive Alcohol Research Center (CARC) mentorship team and the exceptional faculty in the Physiology Department at my institution, will undoubtedly provide me with the resources and support needed to further refine my skills as a physician-scientist.

In conclusion, my passion for translational research, particularly in the realm of alcohol research and its profound impact on pain perception, drives me towards pursuing a combined MD/PhD program. The Ruth L. Kirschstein Institutional NRSA training fellowship, combined with the invaluable support of my mentorship team and the exceptional faculty within the Department of Physiology at my institution, will undoubtedly provide me with the resources to further refine my skills as a physician-scientist. With the fellowship and my training at LSUHSC, I am confident in my journey as a physician-scientist to be filled with exciting discoveries for the advancement of human health through translational research.

Specific Aims Page

- Snapshot of entire project proposal with background and major research aims.
- Aims should be connected but not dependent on the success of each other.
- Introduce specific hypotheses and methods utilized.
- Summary figure to help reviewer understand major goals of the proposal.
- Many reviewers will start here!

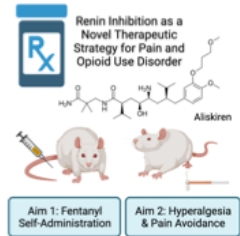
Research Café Date: Nov 11, 2025

Specific Aims

Opioid use disorder (OUD) is characterized by an escalation of opioid use over time and a parallel development of intense negative emotional states. Central to this conceptualization is the continued use of opioids to self-medicate both somatic and emotional pain in individuals suffering from OUD (Pahng and Edwards, 2021). Effective pain management is also a principal aim of medical care, with opioids remaining a frontline resource for analgesia in chronic pain patients. However, opioid exposure directed at alleviating pain can also render individuals more sensitive to nociceptive stimuli, a condition known as opioid-induced hyperalgesia. As a preclinical model of this phenomenon, extended access to self-administered opioids (Edwards et al., 2012), including prescription opioids, produces allodynia/hyperalgesia symptoms in rodents, suggesting a potentiation of pro-nociceptive systems. The elucidation of novel pathophysiological mechanisms driving the escalation of opioid use and subsequent opioid-induced hyperalgesia are desperately needed, spurring the NIH Helping to End Addiction Long-Term (HEAL) initiative to support the early-stage discovery of new pain and OUD targets.

We have identified **renin inhibition** as a highly promising strategy in accord with this initiative, particularly since FDA-approved renin inhibitors are clinically available and well tolerated in most individuals. The renin-angiotensin system (RAS) is a hormone cascade essential for the regulation of blood pressure, although a role in pain has also been described (Bessaguet et al., 2016) including contributions of the brain's RAS (Urmilla et al., 2021). The small molecule renin inhibitor aliskiren (brand names Tekturna and Rasilez) was FDA approved in 2007 for primary hypertension. More recent studies have described a beneficial role for aliskiren to reduce allodynia/hyperalgesia symptoms in a diabetic neuropathy pain model (Alkhudhry et al., 2020), although its effects on opioid-related pain are unknown. Another critical dimension to both OUD and chronic pain is the

ffective or emotional pain component that may be reflected in an exaggerated avoidance of noxious stimuli (Shurman et al., 2010; Massaly et al., 2021). We have characterized an innovative behavioral assay to measure increases in pain avoidance-like behavior and associated neuroadaptations in opioid-dependent animals (Pahng et al., 2017; Pahng and Edwards, 2018). Our more recent work has examined sex differences in voluntary fentanyl use in animals given either extended access (long access, LGA) or limited access (short access, SHA) to fentanyl self-administration (Barattini et al., 2023). We have also confirmed the development and expression of mechanical allodynia in male rats during withdrawal from fentanyl self-administration. With this comprehensive model, we are prepared to meet the urgent challenge presented by the HEAL initiative to directly test our **overall hypothesis that renin inhibition will reduce the escalation of fentanyl self-administration and significantly alleviate hyperalgesia and pain avoidance-like behaviors in fentanyl self-administering animals**. We will test these predictions via two specific aims:



Specific Aim 1 – Test the hypothesis that a renin inhibitor will reduce fentanyl self-administration in animals given extended access to the drug. This aim will incorporate the LGA/SHA model of fentanyl self-administration to determine the efficacy of aliskiren (direct renin inhibitor) to alter escalated fentanyl intake in male and female rats. Experiments within this aim will also measure changes in plasma renin activity (PRA) in male and female rats receiving fentanyl via self-administration or passive administration.

Specific Aim 2 – Test the hypothesis that a renin inhibitor will alleviate mechanical & thermal hyperalgesia and reduce pain avoidance-like behavior during fentanyl withdrawal. This aim will incorporate von Frey (mechanical) and Hargreaves (thermal) measurements of allodynia/hyperalgesia along with a novel mechanical conflict avoidance assay to determine the efficacy of aliskiren to alleviate pain-related symptoms in male and female rats during withdrawal from fentanyl self-administration.

This proposal examines an FDA-approved therapeutic strategy (direct renin inhibition) to serve as a novel therapeutic avenue for the treatment of OUD and pain. These studies will be conducted in a research environment that features substantial expertise in behavioral neuroscience and neuropharmacology within a comprehensive physiology department and drug abuse center that will maximize the translational potential of these and future directions.

Research Strategy

- Provides an expanded layout of:
 - Background & Scientific Premise
 - Discussion of Innovation
 - Preliminary & Feasibility Data
 - Experimental Aims, Limitations, & Alternative Approaches
 - Methods & Statistical Analyses

Research Café Date: Dec 9, 2025

Research Strategy

Excessive Opioid Use and the Paradoxical Worsening of Pain Symptoms Opioid exposure directed at alleviating pain also paradoxically renders individuals more sensitive to nociceptive stimuli, a condition known as opioid-induced hyperalgesia, or in cases where non-noxious stimuli become painful, allodynia (McGinn and Edwards, 2016). In accordance with this hypothesis, opioid exposure or self-administration in rodents leads to allodynia/hyperalgesia that is magnified with chronic or excessive exposure (Edwards et al., 2012). Given that chronic pain is well known to cause both emotional distress and a negative emotional state (Elman et al., 2013), opioid-induced allodynia/hyperalgesia may be an important co-morbidity closely associated with opioid use disorder (OUD) by facilitating negative reinforcement or self-medication processes (Volkow et al., 2019). Shuman and colleagues (2010) have further hypothesized that effective pain management with doses of opioids that are strictly titrated to the relief of pain represents the best treatment strategy from a clinical perspective, whereas any over-exposure to opioids in excessive amounts may lead to the recruitment of opponent motivational processes in terms of both pain (allodynia/hyperalgesia) and negative affect (termed hyperkatifeia). This aligns with DSM-V OUD criteria of escalated opioid use, severe withdrawal symptoms, and attempts to avoid withdrawal symptoms.

Animal Models of Prescription Opioid Use Disorder & Affective Pain A critical breakthrough in the ability to examine negative reinforcement theories of OUD has been the development and refinement of reliable animal models of escalated drug self-administration (Ahmed and Koob, 1998). For example, extended access to heroin self-administration (12h per day; Long Access [LgA]) leads to escalation of heroin intake and dependence in rats, while animals given restricted access (1 h per day; [ShA]) maintain a steady low level of use and may better model recreational drug users (Edwards et al., 2012; Edwards and Koob 2013). Importantly, direct comparison of LgA animals to ShA animals may allow for the revelation of mechanisms associated with the transition from initial opioid use to dependence (Edwards, 2016). Concurrent evaluation of this constellation of behaviors associated with excessive opioid intake allows for a remarkably valid and comprehensive analysis of addiction-related symptomatology with considerable face validity, allowing for the study of basic physiological mechanisms underlying each component as well as the preclinical development of novel therapeutic strategies (Edwards and Koob, 2012). A recent study (Wade et al. 2015) established parameters for ShA and LgA self-administration of the prescription opioid fentanyl in rats. Our preliminary data using these procedures demonstrates a significant development of mechanical allodynia during withdrawal that appears to correlate with fentanyl access (Figure 1). As pain is a multidimensional experience comprised of both somatic sensory and cognitive/motivational/affective components, we have also developed a valuable model of heightened pain avoidance behavior in the context of opioid dependence (Figure 2).

Justification for Targeting Renin Physiology for the Treatment of Pain and OUD A screen associated with a previous HEAL RFA revealed the renin receptor as a part of the understudied druggable proteome. After conducting a comprehensive search of the literature and consulting with our renal physiology and pharmacology colleagues, we considered the best strategy for intervention at the level of this target while incorporating a viable translational approach. While the renin receptor mediates much of the physiological activity of renin on target systems (including angiotensin production; Nguyen et al., 2022), directly inhibiting the receptor is not currently feasible outside of ex vivo application of dominant-negative peptidergic compounds that may not translate well. We instead believe that direct inhibition of renin itself would serve as an effective way to reduce renin receptor activity, and this strategy is all the more promising given our ability to inhibit this system via the FDA-approved therapy aliskiren. Moreover, a comprehensive study (Patel et al., 2013) demonstrated the antinociceptive efficacy of aliskiren (1-50 mg/kg) in the writhing test, formalin hind paw test, capsaicin-induced pain test, and orofacial pain test in mice as well as beneficial effects in models of post-operative pain and neuropathic pain in Sprague-Dawley rats (30-100mg/kg). A more chronic regimen of aliskiren (45 mg/kg per day for eight weeks) also attenuated neuropathic pain in diabetic Sprague-Dawley rats (Alkudhairy et al., 2021), suggesting that analgesic tolerance does not develop with repeated treatment. Another study found that a similar dose range (15-60 mg/kg) reduced systemic inflammatory markers and pathological symptoms in two inflammation models in Wistar rats (Aziz et al., 2020). Less is known about how opioids may regulate renin release and activity. One study in newborns (24-48 hours old) of opioid-dependent mothers revealed hypertension in association with elevated plasma renin activity (Dube et al., 1981). Renin activity was also increased in rats experiencing naloxone-precipitated withdrawal (Delle et al., 1990). There is also considerable evidence for a brain RAS that could be particularly relevant to OUD and the cognitive/motivational/affective dimensions of pain, although the precise mechanisms are controversial (Sigmund et al., 2017) but could be explored in future work.

Elements of the Research Strategy

- Clear figures and experimental design
- Use rhetoric & references strategically
- Put words in the reviewer's mouth:
"This work is innovative because..."
- State limitations of proposal
- List alternative approaches

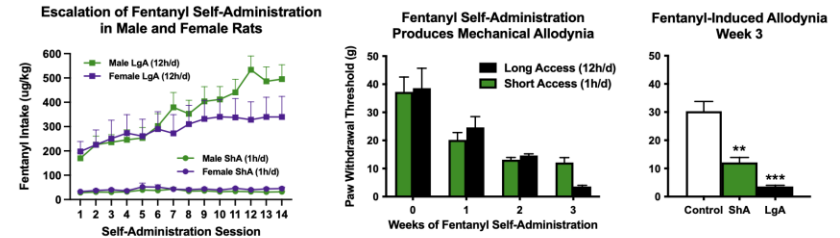
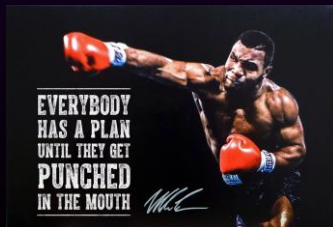


Figure 1. (Left Panel) Animals given short access to fentanyl self-administration (1h/d, ShA) display a relatively low and stable intake. In contrast, both male and female rats given long access to fentanyl self-administration (12h/d, LgA) exhibit an escalation of fentanyl intake (male $n=10-14$ /group, female $n=7-8$ /group; $F_{13,455} = 14.89$; $***p<0.0001$ interactive effect of fentanyl access condition x session). **(Right Panels)** In separate groups of male rats, both ShA and LgA groups exhibit mechanical allodynia symptoms (reduced paw withdrawal thresholds in von Frey tests) that worsen over time, and this effect appears greater in LgA vs. ShA animals. ($n=5-9$ /group, $***p<0.01$ and $***p<0.001$ reduced thresholds in ShA and LgA groups relative to naive controls by Tukey's multiple comparison test following significant main effect of fentanyl access group, $F_{2,17} = 25.54$).

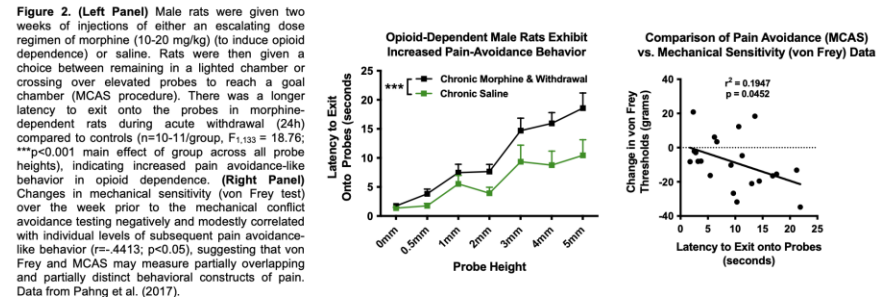
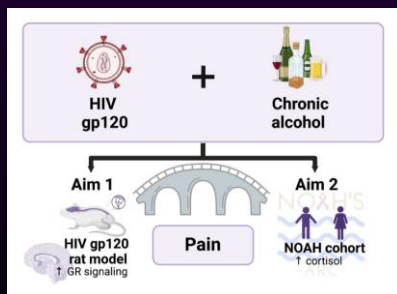


Figure 2. (Left Panel) Male rats were given two weeks of injections of either an escalating dose regimen of morphine (10-20 mg/kg) (to induce opioid dependence) or saline. Rats were then given a choice between remaining in a lighted chamber or crossing over elevated probes to reach a goal chamber (MCAS procedure). There was a longer latency to exit onto the probes in morphine-dependent rats during acute withdrawal (24h) compared to controls ($n=10-11$ /group, $F_{1,133} = 18.76$; $***p<0.001$ main effect of group across all probe heights), indicating increased pain avoidance-like behavior in opioid dependence. **(Right Panel)** Changes in mechanical sensitivity (von Frey test) over the week prior to the mechanical conflict avoidance testing negatively and modestly correlated with individual levels of subsequent pain avoidance-like behavior ($r=-.4413$; $p<0.05$), suggesting that von Frey and MCAS may measure partially overlapping and partially distinct behavioral constructs of pain. Data from Pahng et al. (2017).

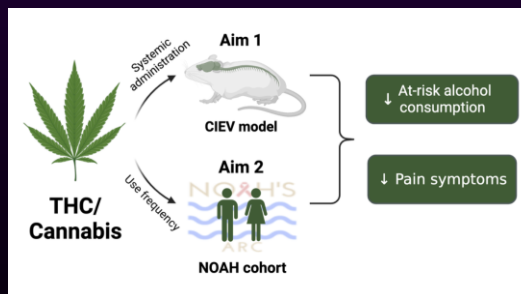
Research Café Date: Dec 9, 2025

Fellowship Specific Aims & Research Strategy

- Contributions from Sponsoring team, including conceptualizations & preliminary data.
- Keep in mind that the research should serve a training purpose in line with your goals.



Taylor Fitzpatrick-Schmidt
F30AA030941

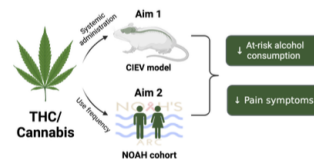


Stephanie Lee
F30AA031900

Specific Aims

Alcohol use disorder (AUD) affects more than 10% of the United States population (SAMHSA, 2023). AUD is a psychiatric disorder characterized by escalated alcohol use and the potentiation of negative motivational states. Alcohol is also well known for its analgesic effects (Thompson et al., 2017), although excessive use leads to increased pain sensitivity (or hyperalgesia) during withdrawal (Edwards et al., 2012, 2020). Chronic pain affects over 20% of the global population and contributes to the development and severity of both psychiatric illness and AUD, although effective pharmacological treatments for these conditions remain severely limited (Rikard et al., 2023). In recent years, many individuals have turned to recreational or medicinal cannabis for management of chronic pain and related health conditions. Specifically, delta-9-tetrahydrocannabinol (THC), the main psychoactive component of cannabis, may offer a promising avenue for treating pain, a common cause of excessive drinking in individuals with AUD. While some support for the motivated use and utility of cannabis to reduce alcohol drinking exists at the clinical level, there is an urgent need to understand both the anti-hyperalgesic efficacy of cannabis/THC in the context of alcohol dependence and how use may either mitigate or worsen the risk of escalated drinking and AUD (Risso et al., 2020).

Our previous preclinical work has shown a functional role for the central amygdala (CeA) in the promotion of hyperalgesia and escalation of alcohol drinking in a preclinical animal model of AUD. As an extension of my NIAAA T35 Summer Research Fellowship examining biobehavioral outcomes of acute alcohol in the context of chronic inflammatory pain (Cucinello-Ragland et al., 2023), I recently analyzed a proteomics data set that compared CeA protein expression in alcohol-dependent vs. non-dependent rats of both sexes. My analysis revealed significant changes in several canonical pathways affected by alcohol, including the endocannabinoid (eCB) neuronal synapse pathway in both sexes. Our findings indicate that chronic alcohol exposure produces a state of endocannabinoid system dysregulation that may underlie the potential therapeutic efficacy of cannabis/THC in individuals suffering from AUD and AUD-related pain. These preliminary results underscore the need for more comprehensive investigations to understand the intricate interplay between the eCB system, pain symptoms, and alcohol use. **My overall hypothesis is that activation of the cannabinoid system will be associated with a reduction in pain symptoms and alcohol use.** This hypothesis will be examined with specific aims combining a preclinical animal model of AUD and a cross-sectional examination of a clinical cohort of cannabis-using individuals that exhibit various levels of alcohol drinking and AUD risk.



Specific Aim 1: Test the hypothesis that delta-9-THC administration alleviates hyperalgesia and reduces escalated alcohol self-administration in alcohol-dependent male and female rats. Using the chronic, intermittent ethanol vapor (CIEV) procedure, I will determine the dose-dependent pharmacological efficacy of delta-9-THC systemic administration on pain-related behaviors (mechanical/thermal hypersensitivity and pain avoidance) and alcohol self-administration in alcohol-dependent rats of both sexes. This work will be guided by Dr. Scott Edwards (Sponsor) and Dr. Nicholas Gilpin (Co-Sponsor), who have a rich collaborative history.

Specific Aim 2: Test the hypothesis that cannabis use is associated with reduced pain symptoms and reduced at-risk alcohol use in men and women. I will utilize both self-reported and empirical measures of mechanical and thermal nociceptive sensitivity to quantify pain symptoms in the NIAAA-funded Comprehensive Alcohol Research Center (CARC; PI Dr. Patricia Molina, Co-Sponsor) New Orleans Alcohol Use in HIV (NOAH) cohort. To determine recent and at-risk alcohol use, I will examine circulating phosphatidylethanol (PEth) levels (objective biomarker of recent alcohol use), lifetime drinking history (LDH), Addiction Severity Index (ASI), and Alcohol Use Disorder Identification Test (AUDIT) scores. To determine the incidence and frequency of cannabis use, I will utilize self-report, ASI, and Cannabis Use Disorder Identification Test (CUDIT) data. Correlational analyses of data from our established baseline cohort (n=365, 31% female) will be followed by more stringent logistical regression and longitudinal analyses to determine important relationships and contributing variables (see Letter of Support from Dr. Tekeda Ferguson, Director of CARC Data Analysis Core).

This research training plan will provide valuable new information on the utility and efficacy of cannabis/THC interventions for the treatment of AUD and related pain symptoms in men and women while facilitating the career development of a future physician-scientist focused on a translational research career in the clinical neurosciences.

Timeline for Proposed Training:

	G2 (2024 – 25)	G3 (2025 – 26)	M3 (2026 – 27)	M4 (2027 – 28)
Research	Experiments and Analysis for Aim 1 & Aim 2		Basic Science & Clinical Seminars	
	Lab Technical and Analytical Skills			
	Preliminary Exam		Dissertation and Defense	
	Manuscript 1	Manuscript 2	Manuscript 3	Manuscript 4
Clinical Training	Monthly Empirical Pain Tests for NOAH Cohort		Clinical Clerkships	
	Biweekly Volunteer at Student-Run Community Clinic (SRCC)			
	Monthly Volunteer with Freestanding Communities (Local Health Outreach Organization)			
	Monthly MD/PhD Forum for Community Building, Clinical Vignettes, and Research Updates			
	Monthly CARC ICC Meetings (Including Dr. Welsh & Dr. Ferguson)			
Professional Development	RSA Conference	ICRS	SEMSS	RSA Conference
	Society for Neuroscience Conference		American Physiology Summit	
	Weekly Student Work in Progress (SWIP) Meetings		Small Group Medical Ethics Discussions	
	Weekly Edwards Lab Meetings & 1-on-1 Meetings with Dr. Edwards		HIPAA Privacy Training	
Coursework	Monthly Co-Sponsors Lab Meetings			
	Perspectives in Alcohol Research		Clinical Courses	
	Weekly Seminar & Journal Club			
	Biostatistics	Responsible Conduct of Research II	Ethics in Biomedical Sciences	
	Scientific Writing	Neurophysiology of Behavior		
	Endocrinology			

Fellowship (F) Research Café Date: May 12, 2026
 Career Development Award (K) Research Café Date: June 9, 2026

Budget & Budget Justification

Business Manager

Budget Justification

Personnel:

Scott Edwards, PhD (LSU Health-New Orleans, 20-15% effort), Principal Investigator: Dr. Edwards has extensive experience using preclinical animal models to investigate the biochemical and behavioral pharmacological mechanisms underlying substance use disorder and will provide scientific direction and managerial oversight for technical staff and any trainees involved in the project in close collaboration with Dr. Amanda Pahng, who he has collaborated extensively with on the procedures contained within this proposal. His laboratory will conduct all behavioral and molecular assay experiments in close coordination and consultation with Dr. Pahng. He will also be responsible for preparation of progress reports, dissemination of findings, and preparation of all associated regulatory protocols.

Amanda Pahng, PhD (Southeast Louisiana Veterans Health Care System and LSU Health-New Orleans, 25-20% effort), Principal Investigator: Dr. Pahng developed the use of the Mechanical Conflict Avoidance System (MCAS) to measure pain avoidance-like behavior in opioid-dependent animals and will consult and guide the conduction and interpretation of behavioral experiments (operant fentanyl self-administration and pain avoidance tasks). Dr. Pahng will also assist in the dissemination of findings and preparation of all regulatory protocols.

Research Associate 1, TBD (LSU Health-New Orleans, 100% effort): Funds are requested for a Research Associate 1 who will oversee and help conduct all surgical procedures, behavioral experiments, and rein activity assays. They will collect, organize, and report the data to Dr. Edwards and Dr. Pahng for analysis and dissemination.

Supplies, travel, and other expenses:

Materials and Supplies: Funds are requested to purchase rodents (n=200) and housing per diems. In addition, funds are requested for IV surgical supplies. Funds are also requested for aliskiren and plasma renin activity (PRA) analyses.

Travel: Funds are requested to support travel for one investigator per year to attend a scientific conference. We anticipate presenting our findings at the Society for Neuroscience.

[illegible]

* MTDC: Exclude Subcontracts over \$25,000 (the first \$25,000 is included in the calculation), equipment, capital expenditures, alterations & renovations, patient care costs, rental costs, participant support costs, student stipends, scholarships, fellowships, and tuition payments. Etc. benefits are included in this calculation.

Research Café Date: Jan 13, 2026

Other Parts of an Extramural Grant App

- Vertebrate Animals & Human Subjects
- Facilities & Resources
- Biohazards and Select Agents
- Authentication of Key Resources
- Data Management & Sharing Plan
- Training in the Responsible Conduct of Research



Research Café Date: July 14, 2026

Office of Research Services

Facilitating timely review of grant proposals, research agreements and research protocols for submission to review committees, sponsors or funding agencies

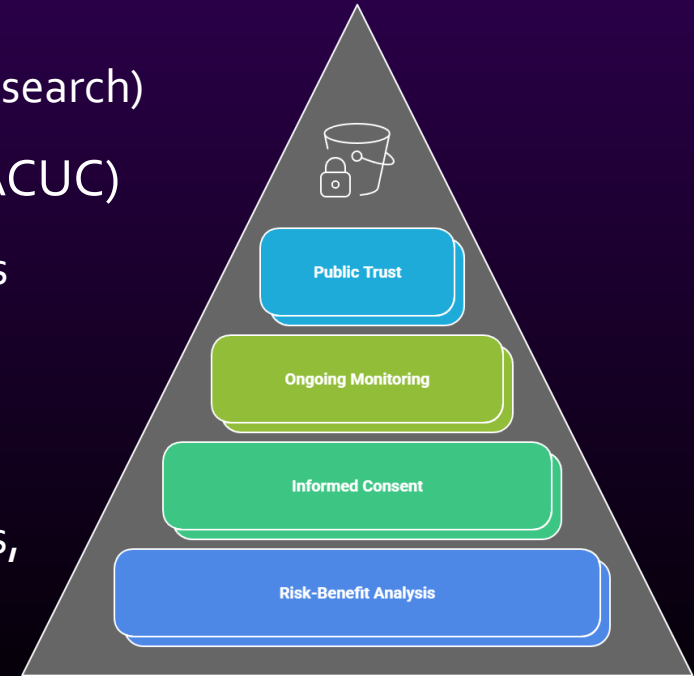
Ensuring conduct of research in compliance with regulatory policies and ethical standards thus safeguarding the rights and welfare of both researchers and human and animal research participants



Institutional Regulatory Bodies

Research Café Dates
IRB – April 14, 2026
IACUC – March 10, 2026
IBC – Feb 10, 2026

- Institutional Review Board (IRB)
 - Human subjects research (including educational research)
- Institutional Animal Care and Use Committee (IACUC)
 - Care and responsible use of live vertebrate animals
- Institutional Biosafety Committee (IBC)
 - Recombinant or synthetic nucleic acid molecules
 - Also pathogens, infectious materials, select agents, biological toxins, and other biohazards



Some Steps to Get Started

Respect and Rely on
Your Colleagues!

- Have your institution register you with NIH eRA Commons
 - eRA Commons ID is required to submit grants
 - eRA Commons will allow you to track grant status
- Appreciate the time it takes to prepare grants & get funded
 - Getting funded can take a year even if everything goes perfectly
 - Respect internal deadlines for processing submissions
 - Utilize departmental and institutional resources for pre-review of grant proposals
 - You can submit six NIH grants per year (recycle preliminary data & diversify targets)



Some Parting Advice: Get a Writing Mentor

- Research abstracts, travel awards & other applications
- IACUC, IRB, IBC applications & amendments
- Thank you notes to visitors & seminar speakers
- Cover letters for manuscript submissions
- Response to reviewer comments (grants & publications)
- Symposium proposals
- Scientific manuscript reviews
- Slide decks for oral presentations – seminar talks & lectures
- Letters of recommendation
- Carefully crafted emails to important or difficult people

Some Examples of
What a Good Writing Mentor
Will Help You With

Few Professionals Received
Formal Training in All of These

