SUPER Program Description

Summer Undergraduate Pharmacology-Experience in Research (SUPER)

Summer Undergraduate Research Fellowship (SURF)

SUPER-SURF Program Overview

The Department of Pharmacology, Toxicology, & Neuroscience at **Louisiana State University Health-Shreveport** will offer an 8-week internship in a research laboratory to provide career opportunities in graduate research in pharmacology, toxicology, substance use, carcinogenesis, chemoprevention, neuropharmacology, and neuroscience. Financial support will be provided ($4,000). Housing costs will also be paid, and participants will be housed at Pilot's Pointe on the Louisiana State University-Shreveport campus (separate from LSUH-Shreveport). All travel related costs including airfare or mileage will also be paid. A weekly career development seminar series will be offered. In addition, students will receive laboratory safety training (including possible chemical and biological hazards), appropriate consideration for safe and humane animal handling, and radioisotope methodology. Each student will have their own project, to be mentored by participating faculty members. At the end of the summer internship, students will present their research findings in a departmental poster session. Students will be required to apply for membership in the American Society for Pharmacology and Experimental Therapeutics (ASPET) and encouraged to apply for student/affiliate memberships in other professional organization such as the Society for Neuroscience, Society of Toxicology, College on Problems of Drug Dependence, or the American Association for Cancer Research. The Program Director will sponsor students for membership in ASPET. Mentors and/or the Program Director will sponsor students for membership in other professional organizations. Students will be contacted on a yearly basis as a follow-up to the program to track their research career. Students will also be encouraged to apply for travel awards to the Experimental Biology meeting to present their posters.

Brief Descriptions of Research Projects*

Faculty member	Research projects
Nicholas E. Goeders, Ph.D.,	Novel pharmacotherapies for substance use disorder; sexual pharmacophysiology of methamphetamine in female rats
Xiao-Hong Lu, Ph.D.	Combining genetics and pharmacology to develop neurocircuit selective therapy for neuropsychiatric disorders.
Kenneth E. McMartin, Ph.D.,	Renal and endothelial toxicity of antifreeze; alcohol and vitamin transport
Kevin Murnane, Ph.D.	Developing new disease modifying treatments for addiction.
Hyung Nam, Ph.D.	Neuropharmacology of alcoholism and psychiatric disorders, neuroproteomics
Armando Salinas, Ph.D.	The neurobiology of motivated behaviors including alcohol and substance use disorders
Christopher Schmoutz, Ph.D.	Neuroendocrinology, behavioral neuroscience, drug addiction, neurochemistry
Yunfeng Zhao, Ph.D.,	Oxidative stress, antioxidants in cancer prevention and treatment

*All students will be expected to conduct an independent research project, under the direct mentorship of the faculty member and/or their most senior students/staff.

Student Activities Available through the SURF Program at LSU Health Shreveport

Interactions occur in the laboratories, at the weekly career development seminar series (below), journal clubs and seminars, and at poster/platform sessions. In addition, regular social opportunities are provided.

Example of Schedule of Topics from the 2022 LSU Health Shreveport Summer Undergraduate Pharmacology Experience in Research (SUPER) Program

Date	Day	Topic	Discussion Leader
June 9	Thurs 9 AM	Overview of what is pharmacology Translational Pharmacology	Nicholas Goeders, Ph.D.
June 10	Fri 1 PM	Ice Cream Social and Welcome!	All faculty, staff and students are welcome!
June 15	Wed 12-12:30	Pharmacogenomics and pharmacometabolomics	Hugh Nam, Ph.D.
June 16	Thurs 12-1	Philosophy, Ethics and the Scientist *1-400 Auditorium	Christopher Schmoutz, Ph.D.
June 22	Thurs 12-1	Cancer Research and Toxicology	Yunfeng Zhao, Ph.D.
June 30	Thursday 12-1	Use of Animals in Biomedical Research *1-400 Auditorium	Christopher Schmoutz, Ph.D.
July 4	Mon 8 AM	Firecracker 5K Run for Research (Optional)	https://www.sportspectrumusa.com
July 7/14	Thurs 12-12:30	The future of brain research	Xiaohong Lu, Ph.D.
July 21	Thursday 12-1	Careers in Science	Kenneth McMartin, Ph.D. Diana Merendino, DPT, RRT, RRT-NPS, RPFT, FAARC
July 28	Thurs 12-1	Overview of graduate school and how to apply	Kevin Murnane, Ph.D. Ty Martinez
July 29	Fri 2-4	Poster Presentation “BRI 5th Floor Atrium”	All faculty, staff and students are welcome!

How students will report their project
Students will be provided with training on how to present a poster session during the weekly Career Development Seminar Series. At the end of the summer session, each student will present a poster based on their research findings. The poster session will be open to all faculty, staff, students, family and friends of the SUPER-SURF students. Refreshments will be provided during the poster session. Students are allowed to take the posters home with them. Many of our current and previous SUPER students have presented their posters back at their home colleges and at regional scientific meetings. Students will also be encouraged to apply for the SURF fellow travel award to present their posters at the Experimental Biology meetings.

Assurances
Laboratory safety training for students is mandatory. Biosafety training and Radiation training is offered. Certifications are given to the students following successful completion of training. Any students working with animals will be required to complete training modules and be added to the mentor's animal protocol. LSUHS has a temperature- and humidity-controlled AAALAC facility with a 12 h light/dark cycle. All procedures will be approved by the LSUHS Institutional Animal Care and Use Committee in accordance with NIH guidelines.

Mechanism for tracking students
The Academic Coordinator writes to each student starting at the end of the summer asking them to voluntarily participate in an anonymous survey (using "FormStack" online). This allows the students to give valuable feedback about the program every year such that we can continue to improve it. After that, Dr. Goeders, the mentors, and the coordinator (Mrs. Ty Martinez) contact the students by phone and/or by e-mail at least once a year, and quite often more than that. Many mentors maintain contact with former SUPER-SURF students for many years. The coordinator is also able to obtain information using electronic media such as "Facebook".

The following pages are examples of former SUPER Student Projects (2022)

Neurogranin expression in human aortal endothelial cells and mouse atrial cardiomyocytes

Benjamin J. Brisky[1,2], Ashton Jorgensen[3], Hyung W. Nam[3]

[1]Dept. of Biological Sciences, Florida Gulf Coast University, FT Myers, FL
[2]Summer Undergraduate Pharmacology Experience in Research (SUPER) Program, LSU Health Shreveport, LA
[3]Dept. Of Pharmacology, Toxicology, and Neuroscience, LSU Health Shreveport, LA

Neurogranin (Ng) is a small (17kDa) regulatory protein which modulates calcium-calmodulin (Ca^{2+}-CaM) signaling and Ca^{2+}-mediated synaptic plasticity in the brain. Despite its reputation as a neuron-specific protein, Ng has been identified in smooth and skeletal muscle, cardiomyocytes, and endothelial cells. Our lab has previously demonstrated that Ng is an important regulator of nitric oxide (NO) signaling in the endothelium and that Ng regulates calcium-dependent hypertrophy in cardiomyocytes. Given the significance of Ng in maintaining proper cardiovascular functioning, it is important to further characterize the role of Ng expression in the heart and vasculature.

In this study, we investigated the subcellular localization of Ng and phospho-Ng (p-Ng) in primary human aortal endothelial cells (pHAECs) and mouse atrial cardiomyocytes (HL-1 cells). Given the importance of Ng as an eNOS regulator, we hypothesized that both proteins would be closely situated within pHAECs. Western blot analysis of cellular fractions indicated that Ng is localized in the cytoplasm, nucleus, mitochondria, and near the cell membrane of pHAECs, while p-Ng is dominantly localized in mitochondria and cytoskeleton. Moreover, eNOS appeared in the nuclear and membrane fractions, and immunofluorescent imaging revealed that Ng and eNOS co-localize near the nucleus and cell membrane in pHAECs. In HL-1 cells, we observed Ng localization in the cytoplasm, near the cell membrane, and in the mitochondria but not in the nuclear fraction. Western blot analysis of HL-1 cell lysates revealed that p-Ng is expressed within the mitochondria and is associated with the cytoskeleton in in the myocardium. Overall, our findings indicate that Ng is concentrated near the nucleus and membranes of pHAECs but diffusely localized in HL-1 cells. We are the first to report the co-localization of Ng and eNOS in pHAECs. Our data suggest that Ng and p-Ng may play a role apart from regulating Ca^{2+}-CaM signaling in maintaining proper mitochondrial functioning in pHAECs and HL-1 cells.

Title: Characterization of Novel Tryptamines' Anxiolytic and Anti-Inflammatory Effects in Relation to their Psychoactive Effects

Authors: Carfagno, Catharine M.[1]; Vest, M. Frances[1,2]; Wood, Bo Jarrett[1,2]; Murnane, Kevin Sean[1,2,3]

[1]Department of Pharmacology, Toxicology, and Neuroscience, LSU Health Shreveport, Shreveport, LA; [2]Louisiana Addiction Research Center, Shreveport LA; [3]Department of Psychiatry and Behavioral Medicine, LSU Health Shreveport, Shreveport, LA

Psychedelics are a class of drugs characterized by their psychoactive properties through primary action of the serotonin system, specifically the serotonin 2A receptor (5-HT2aR). Recent clinical research has shown efficacy for treatment-resistant depression, end-of-life anxiety, and substance use disorders. There are two main classes of psychedelics, phenethylamines and tryptamines, that have slightly different affinities for the various 5-HT receptors, and therefore display slightly different effects. The purpose of the current research is to distinguish the anti-inflammatory, anxiolytic, and psychoactive effects of an established phenethylamine, DOI, and three novel tryptamines, compound 1, 2, and 3, that are structural analogs of psilocybin. To evaluate the anti-inflammatory effects of these compounds, RAW P98 macrophages were exposed to lipopolysaccharide (LPS) and treated with a range of concentrations of each psychedelic. After 24 hours the supernatant was evaluated for NOx levels (Griess assay) and TNF-a (Elisa). To investigate the potential role of the 5-HT2aR in the anti-inflammatory response, the same assays were run using the 5-HT2aR antagonist, M100907. Differences in psychoactive effects were established by the Head Twitch Response (HTR). Differences in anxiolytic properties were established using the elevated zero maze (EZM) with acute and chronic administration of psychedelics, evaluating the role of downregulation of the 5-HT2aR on anxiety. The results suggest that DOI produces the most robust anti-inflammatory response in both NOx and TNF-a assays of all four compounds, while compound 2 showed the most robust anti-inflammatory response out of the three novel tryptamines. In vivo DOI displayed the most robust HTR while also demonstrating robust anxiolytic effects. Of the three tryptamines, compound 1 & 3 had the most robust HTR and anxiolytic response while compound 2 had the inverse. These results suggest that the magnitude of the anxiolytic response relies on the magnitude of the psychoactive effects, but further studies are needed to determine this.

Ethanol effects on synaptic transmission: implications for motor learning and memory

Grace Nelson[1,2], Armando Salinas[3]

[1]Departement of Biology, Kansas State University
[2]Summer Undergraduate Pharmacology Experience in Research (SUPER) Program, LSU Health Shreveport
[3]Department of Pharmacology, Toxicology & Neuroscience, LSU Health Shreveport

Alcohol is one of the most widely used and abused drugs in the United States, with the National Survey on Drug Use and Health reporting that alcohol misuse costs the country 249 billion a year. The majority of these costs are attributed to binge drinking, which 25.8% of surveyed adult participants had recently participated in. One of alcohol's well-known effects is its inhibition of coordination and motor learning during intoxication. The exact mechanism of how alcohol affects motor learning is unknown but is likely linked to the inhibition of excitatory signaling, particularly in the striatum, a brain region essential for coordinated movement. To investigate this effect, excitatory field potentials were measured from acutely prepared mouse brain slices containing the striatum. We first determined that the field potentials were AMPA receptor mediated via the application of DNQX, an AMPA receptor antagonist. Application of DNQX extinguished field potentials. We next examined the effect of ethanol on striatal synaptic transmission and found a dose-dependent inhibition of synaptic transmission. Ongoing efforts will determine how ethanol-mediated inhibition of synaptic transmission affects synaptic plasticity, the molecular substrate of motor learning and memory.

Does Environmental Toxicant Exposure Increase the Susceptibility and Severity of COVID-19?

Adam Trupp[1]; Xinli Tian[1]; Hongbo Zhang[1]; Mychal Grames[1]; Clifton Haacker[1]; Kelsea Keys[1]; Erika Knott[1]; Lu Xiao-Hong[1]

[1] Department of Pharmacology, Toxicology, and Neuroscience, Neurology, Louisiana State University Health Shreveport, Shreveport, Louisiana, USA

Novel Coronavirus (COVID-19) has killed more than 6 million people worldwide since its outbreak in late 2019 and continues to mutate, causing an increase in infection, hospitalization, and death across the globe. According to CDC, 1 out of 5 adults who are infected with COVID-19 develops longer-lasting chronic symptoms termed "long COVID." Persistent symptoms of this so-called "long COVID" are characterized by fatigue, "brain fog," difficulty breathing, heart palpitations, joint and muscle pain, and most notably, death, among other symptoms. According to CDC, more than 1 in 5 adult Covid survivors in the U.S. may develop PASC. Chronic neurocognitive and neurologic symptoms: "brain fog," mood changes, sleep problems, and anosmia/ ageusia are prominent in PASC patients. Aging, underlying disease, and environmental exposure are the main risk factors for the adverse outcomes of COVID-19. However, the common pathogenic mechanism that exists across different demographic characteristics is still unknown. Previous work in our lab supports the hypothesis that persistent genotoxic stress associated with aging and environmental toxicant exposure are pathogenic and may contribute to the susceptibility and severity of COVID-19. To examine the hypothesis, we performed a geographic information system (GIS) study of the COVID-19 death per capita (per parish) in Louisiana to agricultural pesticide exposure. We have identified a significant association between Paraquat and 2,4-D use and the accumulative COVID-19 death in central Louisiana along the Mississippi River. To determine if genotoxic stress is indeed a prominent feature of COVID-19, we next examined six COVID-19 postmortem tissue samples and six control cases. DNA and RNA samples were extracted from postmortem samples. We have identified significant upregulation of genes associated with genotoxic stress in lung tissue, including telomere attrition, inflammation (cytokines), DNA damage response (DDR), and cell senescence biomarkers. Pathology study via immunohistochemical (IHC) staining was performed to examine the DDR, cell senescence, and neuroinflammation with γH2AX, p21, and Iba1 antibodies, respectively. γH2AX, a phosphorylated histone protein that indicates DNA damage response, was increased in the lung and brain of the deceased COVID-19 patients compared to that of the controls. Cell senescence maker p21 also was increased in patients but did not reach statistical significance. Lastly, Iba staining in the patient brain revealed increased cell density and microgliosis, suggesting neuroinflammation. These observations revealed that genotoxic stress is a prominent feature in COVID-19 and could be a mechanistic link between environmental toxicant exposure and COVID-19 susceptibility and severity. Our studies highlight the need for mechanistic and longitudinal studies in animal models to confirm a causal pathogenic role.

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