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 be paid and participants will be housed at Pilot's Pointe on the Louisiana State University-Shreveport campus, and all travel related costs including airfare or mileage will 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.,	Development of novel pharmacotherapies for substance use disorder.
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
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 2021 LSU Health Shreveport Summer Undergraduate Pharmacology Experience in Research (SUPER) Program

Date	Day	Topic	Discussion Leader
June 3	Thurs 9 AM	Philosophy, Ethics and the Scientist *G-420*	Christopher Schmoutz, Ph.D.
June 10	Thurs 1 PM	Ice Cream Social and Welcome!	All faculty, staff and students are welcome!
June 16	Wed 1-2	Overview of What is Pharmacology Translational Pharmacology	Nicholas Goeders, Ph.D.
June 17	Thurs 9 AM	Dissertation Defense	Lailun Nahar
June 24	Thurs 12-1	Use of Animals in Biomedical Research *G-420*	Christopher Schmoutz, Ph.D.
June 30	Wed 12-1	Careers in Science	Kenneth McMartin, Ph.D. Diana Merendino, DPT, RRT, RRT-NPS, RPFT, FAARC
July 3	Sat 8 AM	Firecracker 5K Run for Research (Optional)	https://www.sportspectrumusa.com
July 7	Wed 12-1	The future of brain research Pharmacogenomics and pharmacometabolomics	Xiaohong Lu, Ph.D. Hugh Nam, Ph.D.
July 14	Wed 12-1	Cancer Research and Toxicology	Yunfeng Zhao, Ph.D.
July 21	Wed 12-1	Overview of graduate school and how to apply	Kevin Murnane, Ph.D. Ty Martinez

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 (2021)

A Novel Genetic Biodosimetry for Brain Genomic Instability to Predict Clinical Health Outcomes in Human Spaceflight Crews for Mars Mission

Sarah Aviles[1,2], Erika L. Knott[3], Kelsea Keys[3], Madison Wynne El-Saadi[3], Xinli Tian[3], Jeffery Chancellor[4], Lynn Harrison[5], Xiao-Hong Lu[3]

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A major concern indicated by NASA regarding human missions into deep space is the effects of Galactic Cosmic Radiation (GCR), a type of ionizing radiation, on biological systems. When traveling outside of low Earth orbit, one is outside Earth's protective magnetic shield, increasing the exposure to GCR. The radiation dose estimated from a 3-year Mars mission is 1.2 gray (Gy), compared to a 0.16 Gy dose from a 6-month mission in the International Space Station. An important focus is how GCR affects the neurons of the central nervous system (CNS). It is hypothesized that GCR experienced in deep space missions has the capability of causing DNA damage in neurons, increasing the risk of developing neurodegenerative diseases.

In this study, we have developed a genetic reporter to evaluate brain damage inflicted by GCR. The genetic sensor harnesses the DNA damage-dependent viral transduction in postmitotic neurons, the instability of varying lengths of microsatellite DNA sequences and membrane-tethered multi-color fluorescent proteins to identify postmitotic neurons undergoing genomic instability. The design incorporates membrane tethering farneslyated/mesylated derivatives of Red Fluorescence Protein (RFP) mScarlet, Green Fluorescence Protein (GFP) mWasabi, and Blue Fluorescence Protein (BFP), with mononucleotide tracts 34G, 22G, and 13G inserted in between the ATG and open reading frame of each FP to create the frame-shift mutations. Cre mediates recombination allowing the mosaic expression of mScarlet, fWasabi, or fBFP. Galactic cosmic radiation-driven DNA instability of the mononucleotide repeat renders the out-of-frame G3n+1 to undergo a frameshift mutation, and therefore the expression of the XFPs marker to label cells. When crossed with the Cre driver lines (e.g., Tyrosine Hydroxylase (TH) Cre mice), the XFPs expression will be limited to DA neurons. Because the mutation rates are inversely correlated with the lengths of the mononucleotide repeat, our design can report three different ("high, medium, and low") levels of DNA instability. To validate the sensor, we have treated HEK 293 cells with Bleomycin, a drug used in cancer therapy, to mimic the effects of GCR. Transgenic mice who contained Cre recombinase driven by the promoter of CamkII, Drd1, or TH were used for in vivo validation. These three types of neurons are the most vulnerable to neurodegenerative diseases such as Alzheimer's, Huntington's, and Parkinson's disease. The mice confirmed to be transgenic were injected with sensors designed to fluoresce in the presence of DNA damage. These mice will receive whole-body exposures to heavy-charge particle radiation to stimulate GCR on Martian surface at Brookhaven NASA Space Radiation Laboratory. Determining the effects of GCR on the CNS could provide a further understanding of the pathogenic mechanism that can lead to the development of biologic counter-measures.

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Proteomics Analysis of the Effects of UCP2 Knockdown on Gallbladder Cancer Cells

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Uncoupling protein 2 (UCP2) plays an important role in maintaining energy and redox balance and is often upregulated in human cancers. Our early studies have demonstrated that UCP2 is highly expressed in human gallbladder tumor tissues, and knockdown of UCP2 suppresses gallbladder cancer cell growth *in vitro* and *in vivo*. To identify which cellular pathways are regulated by UCP2, we performed proteomics analysis using UCP2 knockdown and control gallbladder cancer G415 cells. Our results showed that there were 269 proteins upregulated and 261 proteins downregulated based on the abundance ratio of the samples ($p < 0.05$). 33 pathways were affected by UCP2 inhibition including glycolysis, phosphorylation, and glucose and lipid metabolism. We further performed Western blot analysis and the data confirmed some of the proteomics results. Overall, our results have identified pathways that are regulated by UCP2 which will be studied in future experiments.

Eutylone Produces Anxiety and Self Injurious Behavior Unlike Methamphetamine

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Illicit drug markets have seen an increase in new psychoactive substances in recent years. The speed at which these substances are engineered causes a lack of knowledge on the adverse effects and allow avoidance of government regulations, leading to a higher chance of overdose or death. Eutylone, a synthetic cathinone, belongs to a family of stimulants that also includes cocaine and amphetamines. Eutylone was the most commonly recovered cathinone in drug samples in 2020, accounting for 77% of cathinone identifications. The chemical similarity to conventional stimulants coupled with rapidly increasing prevalence rate creates a need for characterization in order to better understand the safety profile of eutylone. In order to accomplish this, we have used a holistic topographical approach and administered differing doses of methamphetamine and eutylone to subsequently perform locomotor activity studies to compare the effects and dangers of these eutylone. We hypothesize that eutylone shows a narrower therapeutic window when compared to methamphetamine, increasing the possibility of self-injurious behavior or overdose. With the data collected we hope to highlight the unique adverse effects of eutylone in order to prevent further use of eutylone.

Exploring Social Reinforcers in Zebrafish Using Operant Conditioning

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Zebrafish (*Danio rerio*), a shoaling species native to Southeast Asia has become an alternative to mammalian models as it possesses many advantages for biomedical research: a fully sequenced genome, low-cost maintenance, and high fecundity. In addition, a highly developed central nervous system and behavioral repertoire has positioned them as key subjects in experiments in neuropsychiatry, behavioral neuroscience, and neuropharmacology. Despite a burgeoning understanding of their cognitive abilities, few reports of operant conditioning have been published and replicated. This study hypothesized that isolating zebrafish would alter their social interactions and their propensity to work for a social reinforcer. A novel, wireless operant conditioning device was used to present a video of shoaling conspecific zebrafish upon correct response. In addition, social preference and aggression were quantified before and after isolation. While individual tank performance was variable, several density and gender differences emerged during different experimental parameters. Future research of social and visual stimuli in operant conditioning is needed and important impacts of isolation should be explored.

The Role of Hydrogen Sulfide and the Transsulfuration Pathway in Alcohol Use Disorders

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Although there are many potential detrimental effects, alcohol is abused by many individuals throughout the world. Alcohol Use Disorder (AUD) is characterized by frequent, excessive drinking and has many potential ramifications under prolonged exposure, including oxidative stress, liver damage, and death. Our previous data found that blood plasma hydrogen sulfide levels are significantly increased in individuals with preexisting AUD. Hydrogen sulfide (H_2S) is an endogenously produced gaseous transmitter that has recently been studied for its role against reactive oxygen species (ROS), decreasing oxidative stress. Little is known about the role of heavy alcohol consumption in hydrogen sulfide's mechanisms and production. This study attempts to address why individuals with AUD have higher levels of H_2S in their blood plasma. In order to address this question, we studied blood metabolomics using Liquid chromatography–mass spectrometry (LC-MS/MS). We analyzed human blood samples from 36 control and 26 AUD cohorts. We measured the blood plasma levels of 7 metabolites within the methionine cycle and transsulfuration pathway, including methionine (Met), S-Adenosylmethionine (SAM), S-Adenosylhomocysteine (SAH), homocysteine (Hcy), cystathionine (Cysta), cysteine (Cys), and glutathione (GSH) in each sample. To quantify these metabolite changes in AUD cohorts compared to control, 50μL of each cohort's plasma was derivatized using AccQ-Tag and identified by multi-reaction monitoring (MRM) in LC-MS/MS. Among 7 target metabolites, we found a significant increase in blood plasma Met levels and a significant decrease in blood plasma Cys levels in AUD samples. However, there was no statistical difference between Hcy levels in control vs AUD plasma. The changes in blood plasma levels of SAM, SAH, Cysta, and GSH were unable to be detected by this method. Alteration of Met levels and its proceeding metabolites has shown to play a vital role in the development of alcohol induced liver damage. Proper function of the liver is crucial for H_2S regulation by maintaining a high capacity for its clearance. By altering the metabolite levels of the methionine and transsulfuration pathway, the liver function and H_2S levels may be subsequently impacted.