21st Annual Meeting

LBRN

Louisiana Biomedical Research Network

January 20-21, 2023

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21st ANNUAL MEETING OF THE LBRN – 2023

Day 1 : Friday January 20th, 2023

Registration for All Opens (SVM Lobby)	9:00 AM

LBRN Technology and Core Resources Session (Auditorium)*

*Note: This session is separate from the main conference. To register, you must opt-in on the regular registration form. Today's lunch is only provided for registered attendees of this session.

MCBR Core Technology Session

Yong Lee: Overview of MCB services available through LBRN connections	10:00 AM – 10:15 AM
Gianluca Veggiani: Services through Protein Laboratory	10:15 AM – 10:30 AM
Marilyn A Dietrich: Principles and biomedical applications of flow cytometry	10:30 AM – 10:45 AM
Basel H. Abuaita: Principles and applications of Seahorse	10:45 AM – 11:00 AM

BBCB Core Technology Session

Chris Taylor: Introduction and Overview of BBC Core	11:00 AM – 11:10 AM
Elia Brodsky: Pine Biotech Educational Programs & Analysis Pipeline	11:10 AM – 11:30 AM
Emmanuelle Ruiz: RNA-Seq Analysis & Ingenuity Pathway Analysis (IPA)	11:30 AM – 11:45 AM
Le Yan / Nayong Kim: Computing Infrastructure & Computational Bootcamps	11:45 AM – 12:00 PM
Boxed Lunches and Q&A with MCBR and BBC Cores	12:00 PM – 1:00 PM

Main Conference (Auditorium)

Introduction (Welcome Remarks): Kousoulas/Stanfield/Dean Garden	1:00 PM – 1:10 PM
Keynote: Carrie Robison, Deputy Commissioner for Sponsored Programs, Louisiana Board of Regents **"Louisiana's Commitment to Biomedical Research and Training"**	1:10 PM – 2:00 PM
FLASH TALKS: Summer Research Graduate Students (6 minutes each) Annika Beaverson, Brook Diehl, Ankit Patel, Hailey Brokenberry, James Hines, Shilpa Thota, Pooma Sai Vaddi, Zachary Wiggins	2:00 PM – 3:00 PM
Break: Refreshments	3:00 PM – 3:10 PM
Keynote: John Stewart, MD, PhD, Director LSUHSC Cancer Center **"The Development of Oncolytic Viral Approaches to Cancer: A Historical Perspective and Current Opportunities"**	3:10 PM – 4:00 PM

Day 1 : Friday January 20th, 2023 (continued)

Poster Sessions and Refreshments (First Floor LSU-SVM)

*Appetizer Table and Wine & Beer Bar will open during this session at 4:30. Bar provided by Dean Garden.

Poster Session 1 (Even Numbered Abstracts) See Annual Meeting Program for Poster Listing	4:00 PM – 5:00 PM
Poster Session 2 (Odd Numbered Abstracts) See Annual Meeting Program for Poster Listing	5:00 PM – 6:00 PM

Dean's Address and Celebration

Introduction: Stephen J. Cutler (Auditorium)	6:00 PM
Dean Garden: Champagne Toast (Auditorium) **Keynote: Oliver Garden, Dean of LSU School of Veterinary Medicine** **"Innovating in the Age of One Health"**	6:05 PM
Dinner (First Floor LSU-SVM) **"Celebrating the Impact of LSU A&M NIH:NIGMS IDeA Programs"** Catered by BRQ	6:30 PM – 8:00 PM

Day 2 : Saturday January 21st, 2023

Auditorium Opens with Breakfast	8:00 AM
Welcome: LSU Administration/EAC	8:15 AM – 8:30 AM
Pilot Project: Nektarios Barabutis "Protective role of Growth Hormone Releasing Hormone Antagonists in Endothelial Barrier Dysfunction"	8:31 AM – 8:41 AM
Pilot Project: Anthony Walker "Formulation and characterization of pluronic lecithin organogel as an efficient transdermal delivery vehicle of the flavonol fisetin and its potent derivatives"	8:42 AM – 8:52 AM
Pilot Project: Cory Coehoorn "Impact of rapid heat acquisition on neural function, decision-making, stress, and inflammation"	8:53 AM – 9:03 AM
Pilot Project: Kazim Sekeroglu "A Multi-View Spatiotemporal Hierarchical Deep Fusion Learning Model for Decoding Human Brain Activity"	9:04 AM – 9:14 AM

Day 2 : Saturday January 21st, 2023 (continued)

Translational Project: Santosh D'Mello "Preclinical Development of Small Molecule Therapeutics for Alzheimer's Disease"	9:15 AM – 9:25 AM
Break: Refreshments	9:25 AM – 9:30 AM
Keynote Speaker: Rafael E. Luna, PhD, Boston College **"The Art of Scientific Storytelling"**	9:30 AM – 9:55 AM
Full Project: Vladimir Kolesnichenko "Nano particulate magnetic imaging Agents for Cancer Diagnostic"	10:00 AM – 10:25 AM
Break: Refreshments	10:25 AM – 10:40 AM
Full Project: Georgios Matthaiolampakis "miR-mediated Inhibition of Lung Cancer Progression"	10:40 AM – 11:05 AM
Full Project: Siva Murru "Development of Pyrazoles and Related Heterocyclic Compounds as Anti-Cancer Agents: Design, Synthesis and Anti-cancer Activity Studies"	11:10 AM – 11:35 AM
Full Project: Kyle Piller "Life in the fast lane: Testing for congruence among transcriptomic signatures"	11:40 AM – 12:05 PM
Break: LUNCH	12:05 PM – 1:05 PM
Full Project: Mary Caldorera-Moore "Multifunctional Living Stem Cell-Laden Hydrogel Networks for Directed Tissue Regeneration"	1:05 PM – 1:30 PM
Full Project: Jean Christopher Chamcheu "Development of fisetin as a novel inhibitor co-targeting PI3K/AKT/mTOR/Rac1 and IL-17A for Treating Psoriasis"	1:35 PM – 2:00 PM
Full Project: Vonny Salim "Elucidation of Plant-Derived Drug Biosynthetic Pathways and Molecular Mechanisms as Anticancer Agents"	2:05 PM – 2:30 PM
Full Project: Omer Soysal "MindPrint: Exploring uniqueness of individuals' brain signals"	2:35 PM – 3:00 PM
Awards and Closing Remarks	3:05 PM – 3:20 PM

Closed Door:

EAC Meet with Steering Committee (LSU-SVM 1212C)	3:25 PM – 4:10 PM
EAC Dinner with Steering Committee (Drusilla Seafood)	6:00 PM – 8:00 PM

Keynote Speakers

Carrie Robison

Deputy Commissioner for Sponsored Programs

Louisiana Board of Regents

"Louisiana's Commitment to Biomedical Research and Training"

Carrie Robison, Deputy Commissioner for Research and Sponsored Initiatives, has a B.A. from Mount Holyoke College in English and Medieval Studies (1991) and graduate degrees from Yale University in English Language and Literature.

She has been with the Board in the Sponsored Programs section since 2001, having previously taught as an adjunct as LSU A&M. From 2001 through 2010, she worked as Special Programs Manager, managing the Graduate Fellows, Awards to Louisiana Artists and Scholars, and Post-Katrina Initiative Support Fund programs and working with unit leadership on strategic planning, development of a statewide research plan, and implementation of CDBG post-Katrina research and education funding. In 2010, she was appointed Associate Commissioner for Sponsored Programs Administration, responsible for day-to-day administration of the Board of Regents Support Fund, and in 2016 she was named Deputy Commissioner for Sponsored Programs. In this capacity, she is responsible for all work of the Sponsored Programs Section. She has assisted with or led implementation of new programs and comprehensive program evaluations and coordinated the restructuring of the Support Fund in 2016. Ms. Robison also participates in development of policies related to higher education research and innovation.

John Stewart, MD, PHD

Director

LSU Health Sciences Cancer Center

"The Development of Oncolytic Viral Approaches to Cancer: A Historical Perspective and Current Opportunities."

Dr. John H. Stewart, IV, MD, MBA, is the founding director of the Louisiana State University- LCMC Health Cancer Center. He also holds the rank of professor of surgery at the Louisiana State University New Orleans School of Medicine. Under his leadership, Dr. Stewart sets the overall mission, vision and direction for multidisciplinary cancer care and cancer clinical research programs for LSU Health New Orleans and LCMC Health.

Before he arrived at LSU, Dr. Stewart served as the deputy director for the University of Illinois Cancer Center and physician executive for oncology services for the University of Illinois Health System. He was also a member of the initial class of Presidential Scholars for the University of Illinois. Dr. Stewart's previous leadership roles include serving as the chief of surgery at the Durham VAMC, vice-chair in the Wake Forest School of Medicine Department of Surgery, and associate dean for clinical research and innovation at the Wake Forest University School of Medicine.

Dr. Stewart received his medical degree from Howard University and completed his general surgery residency at the Vanderbilt University Medical Center. He completed fellowships in surgical oncology, tumor immunology, and molecular oncology at the National Cancer Institute. Dr. Stewart has established a national profile in education, scientific research, and cancer care delivery to underserved populations. His clinical interests are in general surgical oncology, focusing on melanoma, tumor immunotherapy, and peritoneal surface malignancies.

Dr. Stewart serves as a director for the American Board of Surgery, the chair of the American College of Surgeons Advisory Council for General Surgery, and a member of the Halsted Society Board of Directors. Best Doctors, Top Doctors, and Top Surgeons have recognized Dr. Stewart for his patient care achievements. In addition, the National Cancer Institute, Amgen, and the Robert Wood Johnson Foundation have funded his research efforts.

He has published over 100 manuscripts in peer-reviewed journals, including Cancer, Annals of Surgery, JAMA Surgery, the Journal of the American College of Surgeons, the Journal of Thoracic and Cardiovascular Surgery, the Journal of Immunotherapy, Annals of Surgical Oncology, the Journal of Surgical Research, Transplantation, Surgery, and Cancer Gene Therapy.

Oliver A. Garden
BVetMed, PhD, FCPP, FRCVS, DACVIM, DECVIM

Dean

Louisiana State University School of Veterinary Medicine

"Innovating in the Era of One Health Through IDeAs."

Dean Garden's primary research interest focuses on mechanisms of peripheral tolerance in health and disease, spanning the mouse, rat and dog model species of both autoimmune disease and cancer. His work has interrogated the role of regulatory T cells and more recently myeloid-derived suppressor cells in this context.

Garden received a Bachelor of Science in pharmacology with basic biomedical sciences from King's College London, U.K. in 1990, a Bachelor of Veterinary Medicine from the Royal Veterinary College, U.K. in 1993, and a Doctor of Philosophy in gastrointestinal immunology from the Royal Veterinary College in 1998.

In addition to the University of Pennsylvania School of Veterinary Medicine, Garden has served in positions at the Royal Veterinary College, University of South Carolina, Cornell University, and Imperial College London, U.K., and as visiting professor at Queen Mary University of London. He holds numerous specialty qualifications, including Board certification in small animal internal medicine by the American and European Colleges of Veterinary Internal Medicine, both Specialist and Fellowship status of the Royal College of Veterinary Surgeons, and Fellowship of the Higher Education Academy.

Rafael E. Luna, PhD

Associate Dean

Morrissey College of Arts and Sciences

"The Art of Scientific Storytelling"

Rafael E. Luna, Ph.D., serves three leadership roles at Boston College: 1. Associate Dean in the Morrissey College of Arts and Sciences, 2. Director of the Pre-Health Program, and 3. Director of the Gateway Scholars Program for STEM, which provides advising to 1st generation and underrepresented minority students to inspire them to continue in STEM fields.

Dr. Luna earned his bachelor's degree in Biological Sciences from Southern University (Historically Black College and University) in Baton Rouge, Louisiana. During his junior year at Southern, he was one of six individuals selected from a nationwide competition to participate in the inaugural Biomedical Research Training Program at the National Heart Lung and Blood Institute at NIH, which ignited a passion for biomedical research. Dr. Luna thoroughly enjoyed his biomedical research experience, as he subsequently earned his doctorate in Biological Sciences at LSU.

Dr. Luna performed his postdoctorate research at Harvard Medical School, which centered on elucidating the sequence of protein-protein interactions leading to the decoding of the initial start codons of messenger RNAs. Dr. Luna held the position of Instructor in the Department of Biological Chemistry and Molecular Pharmacology at Harvard Medical School. He also held the role as Program Director for Senior Faculty Promotions in the Office for Faculty Affairs at Harvard Medical School. As the previous Executive Director of the National Research Mentoring Network (NRMN) and the former Principal Investigator of the Administrative Core of NRMN located at Boston College, Dr. Rafael E. Luna utilized data analytics to strategically grow NRMN and effectively reach all 50 states, including Hawaii, Alaska & Puerto Rico.

In addition to serving as a leader in higher education, Dr. Luna is the author of the book, The Art of Scientific Storytelling, which provides a narrative roadmap for scientists publishing in peer-review journals. He is a dynamic speaker and has taught his Scientific Storytelling method throughout the United States, Europe and Asia, e.g. Harvard Medical School, Harvard University, Massachusetts Institute of Technology, MIT-Koch Institute for Integrative Cancer, Wyss Institute at Harvard, Harvard University, Children's Hospital-Boston, Brigham & Women's Hospital, Boston University Medical School, Dana- Farber Cancer Institute, University of Bergen (Norway), Saarland University (Germany), University of Graz (Austria), University College of London (England), Beijing (China) and many more.

Abstracts for Oral Presentations by Faculty and Students

FLASH TALKS **Friday, January 20th 2:00 PM – 3:00 PM**
Summer Research Students

Development of green methods for the synthesis of drug scaffolds

Annika Beaverson, Danielle E. Allen and Mark L. Trudell
Department of Chemistry, University of New Orleans

Abstract: Diaryl ketones are often privileged structures and used drug scaffolds in variety of medicinal chemistry applications. As part of broader program at UNO aimed at developing "green chemistry" for organic synthesis, conditions were developed for the preparation of diaryl ketones using a heterogenous palladium catalyzed Suzuki-Miyaura cross-coupling reaction between an aroyl chloride and an aryl boronic acid. The catalyst employed for these reactions was a nanocomposite material of palladium nanoparticles encapsulated in the natural clay halloysite (Pd@Hal). The reactions were performed with several aroyl chlorides and boronic acids in water-alcohol mixtures. These conditions afforded good yields of the corresponding diaryl ketones. The scope and limitations of Pd@Hal catalyzed cross-coupling reaction between aroyl chlorides and aryl boronic acids will be presented.

The Basic Emergency Guidance Instrument: A Training Device for Bag Mask Ventilation

Ankit Patel, J. Stephen Alexander, Luke White, Marjan Trutschl, Philip C.S.R Kilgore, Urska Cvek
Laboratory for Advanced Biomedical Informatics, Department of Molecular and Cellular Physiology, LSU Health Science Shreveport

Abstract: Over-bagging or too frequent delivery of breath is frequently a result of failing to perform manual respiration using an AMBU bag. Bag Mask Ventilation (BVM) is a notoriously difficult skill to master, and although it is most often required in emergency situations, improper utilization of BVM can exacerbate a patient's condition or even lead to patient death. The Basic Emergency Narrated Guidance Instrument (BENGI) is an airflow monitor aimed at training medical personnel to avoid these injuries. We took measurements from participants who provided a per training sample, trained with the device, and then waited a two-week period for the post training. Delivering between 300 mL and 600 mL tidal volume or 8 to 15 breaths/min respiratory rate was considered adequate ventilation for the purpose of assessing performance. We compared the users that trained with the BENGI for a four-day period to users that did not. We observed a statistically significant improvement in the tidal volume and respiratory rate.

Identification of neuroprotective compounds using a model of oxidative stress-induced cell death

Autumn Sanderson, Dylan Roberts, Hailey Brokenberry, and Santosh D'Mello
Department of Biological Sciences, LSU Shreveport

Abstract: The pathogenesis of neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis, involves complex cellular and molecular mechanisms. Among these are oxidative stress, a process that begins in mitochondria but that results in the damage of intracellular macromolecules. We are using the SH-SY5Y neuroblastoma cell line, a cell line commonly used to study mechanisms underlying Parkinson's disease (PD) to identify small molecule compounds that could be developed for the treatment of PD. We find that treatment of SH-SY5Y cells plated at a confluence of about 30% with hydrogen peroxide (H2O2) resulted in cell death in a dose-dependent manner when quantified at 24 hours after treatment. Cell death was substantial at concentrations above 0.25 uM cell death with almost 100% cell death at 1 uM. We are in the process of refining this paradigm of cell death. As observed in SH-SY5Y cells, treatment of HT22 cells, a hippocampally-derived mouse neuroblastoma cell line, with doses of H2O2 of 0.25 uM and higher also produced a substantial amount of cell death. We will also describe results using two compounds that preliminary results indicate might possess neuroprotective effects in this paradigm. These compounds are SU6656, a Src inhibitor, and an inhibitor of PKR.

Twinned Crystal Structure of N-(4-Methoxy-3-nitrophenyl)acetamide

James Hines, Ogad A. Agu , Curtistine J. Deere , Frank R. Fronczek , and Rao M. Uppu
Southern University and A&M College, and Louisiana State University

Abstract: 4-Alkoxyacetanilides (4-AAs), in particular phenacetin, are mostly cleaved to give N-(4-hydroxphenyl)acetamide, the clinically relevant analgesic, while a small portion may undergo deacylation producing carcinogenic, kidney-damaging 4-alkoxyanilines. There has been extensive information on phase I and phase II biotransformation of 4-AAs, but little is known about their biotransformation by non-enzymatic mechanisms including those mediated by nitric oxide-derived oxidants. Toward understanding these processes and shedding light on molecular targets, we have synthesized N-(4-methoxy-3-nitrophenyl)acetamide by acetylation of 4-methoxy-3-nitroaniline using acetic anhydride and purified by recrystallization from water. Single crystals of N-(4-methoxy-3-nitrophenyl)acetamide grown from water were analyzed by X-ray diffraction using Bruker Kappa APEX-11 Duo diffractometer. It was found that N-(4-Methoxy-3-nitrophenyl)acetamide crystallizes in monoclinic space group P21/n with Z=4 with a disordered nitro group in twinned crystals. Refinement using low temperature (90K) X-ray diffraction data yielded R=0.059 for 1675 reflections and 160 parameters. Both the methoxy group and the acetamide groups are nearly coplanar with the phenyl ring, with respective torsion angles of 0.0(4)° for C-C-O-Me and 4.9(4)° about the C-N bond to the ring. The C-N-C-O torsion angle is also insignificantly different from zero, 0.2(4)°. Overall, the 12-atom methoxyphenylacetamide group is coplanar to a mean deviation of 0.042 Å. The nitro group is twisted out of this plane by about 30°, disordered into two orientations with opposite sense of twist. The dihedral angle between the two disordered C-NO2 planes is 59.2°. The N-H group donates intermolecular hydrogen bonds with N...O distance 3.122(4) Å to nitro oxygen at x-1/2, 1/2-y, z-1/2, forming chains in the [1 0 1] direction. Interestingly, the amide carbonyl oxygen atom is not involved in hydrogen bonding. Combined with the recent revelations of mechanisms of action of N-(4-hydroxyphenyl)acetamide through indirect activation of CB1 receptors by 4-aminophenol and endocannabinoid reuptake inhibitor AM 404, the information presented here may provide useful insights into molecular targets for 4-AAs and their nitrated metabolites.

Role of DAMPs in regulating Inflammation and Autophagy process in Pentachlorophenol Challenged Lung and Liver Epithelial Cells

Shilpa Thota, Rizwana Begum, Nandini Bidarimath, WC. Dorsey, Sanjay Batra
Southern University and A & M college, Grambling State University

Abstract: Pentachlorophenol (PCP) was a widely used organochlorine pesticide and wood preservative in the U.S. Due to its carcinogenic activity, the use of PCP was restricted by EPA. PCP is easily absorbed through the skin and lungs. Since it is an environmental toxicant, chronic exposure leads to severe lung and liver toxicity in humans. There are few reports which demonstrate PCP-mediated increase in inflammatory responses and autophagy in various study models. The autophagy process plays a critical role in regulating the expression of inflammatory mediators, protein homeostasis, and cell survival. However, the associated molecular mechanisms are yet to be explored in detail. We used human lung adenocarcinoma cells (A549) and human liver carcinoma cells (HepG2) challenged with 1 and 10μM PCP for 24h as our study model. Our findings demonstrate increased production of cytokines/chemokines; production and release of danger-associated molecular patterns (DAMPs) including heat shock protein 70 (Hsp70) and High mobility group box protein 1 (HMGB1); and expression of several autophagy proteins (Beclin-1, LC3B, ATG12, ATG16) by PCP-challenged A549 and HepG2 cells. We thus hypothesized that DAMPs play a critical role in regulating the autophagy process in PCP-challenged lung and liver cells. In this regard, we observed molecular interactions between Hsp70, TLR4, and Beclin1 in PCP-challenged A549 cells. Furthermore, antibody-mediated neutralization and knockdown of Hsp70 showed abrogated-1) cytokine/chemokine (IL-6, IL-8) production; 2) expression of transcription factors (NF-kB, STAT3) and autophagy-related proteins (Beclin1 and LC3B) in PCP-challenged cells. Our results will provide important information about molecular events responsible for regulating the autophagy process during PCP exposure in our study model(s).

Changes in enzymes of hepatic fibrosis and function of SD rats fed high cholesterol and high methionine diets

Poorna Sai Vaddi and Subramanyam Murthy
College of Sciences and Engineering, Southern University and A & M college

Abstract: Non-alcoholic fatty liver disease (NAFLD) affects approximately 30% of the population World over, and it is soon projected to become a leading cause of chronic liver disease. Fat accumulation in liver or simple steatosis progresses to non-alcoholic steatohepatitis (NASH) to cirrhosis and could culminate in hepatocellular carcinoma (HCC). High dietary Cholesterol (Cho) and Homocysteine, formed from Methionine (Met) are known risk factors for inflammatory conditions like NAFLD and atherosclerosis. Excessive consumption of foods rich in both Cho and Met (dairy, poultry and meat) are rich in both Cho as well as Met and are extensively consumed in the US., and can contribute to the probability of developing, and progression of NAFL/NASH. Dietary intervention and healthy choices have been documented to facilitate the reversal of NASH to steatosis and recovery. Since the combined effects of feeding a dietary excess of Met and Cho, especially in the hepatic context are almost non-existent, the PI's lab conducted studies using adult male SD rats. The rats were fed a) control diet, b) a diet enriched with 1.5% Met or c) 2.0% Cho or d) a combination of 1.5% Met and 2.0% Cho for 35 and 98 days (short and long-term). We saw induction of genes of inflammation and oxidative stress only in rats fed high Cho with rats on Met

showing no changes. The rationale for using the combination diet of Met+Cho was to investigate if there would be an additive effect of inflammation. Hepatic inflammation was seen only in rats fed high Cho, and Met when added to Cho, countered the hepatic inflammation. To alleviate inflammatory responses seen in high Cho fed rats, we tested sitagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor and an antidiabetic drug with several beneficial effects. Instead of lowering, sitagliptin exacerbated hepatic inflammation in rats on high Cho. However, in the combination diet such exacerbations were not found mainly due to the presence of Met, corroborating the beneficial effects of Met even further. Multiple parameters of inflammatory processes were evaluated at gene, protein and structural levels, and the results were corroboratory1-3. The ongoing studies include the analysis for concomitant hepatic functional alterations and analyzing for related mechanistic aspects of fibrosis. Data on increases in liver pathology of high Cho fed rats, and countering of such responses by Met will be presented.

GleIF4A and its interactions with the subcomplex GleIF3b/3g/3i in Giardia

Zachary Wiggins, Tim Mcmahan, Srinivas Garlapati
Department of Biology, University of Louisiana at Monroe

Abstract: Giardia lamblia is a flagellated protozoan human parasite that causes gastrointestinal giardiasis in humans and is responsible for many waterborne outbreaks of diarrhea in the United States. Due to the rise of resistant strains against common drugs such as Metronidazole (Flagyl) and its derivatives, a new approach is needed to treat Giardia. A novel area of study is protein synthesis machinery in Giardia, which has significant differences when compared to its mammalian hosts and could serve as a potential target for future drug therapy. Giardia lacks detectable homologs eIF4G, 4B, and 4H, has smaller 80S ribosomes, and an unusually short 5' untranslated region (0-6 nucleotides). eIF4G exists as a complex with cap binding protein eIF4E and RNA helicase eIF4A and is responsible for recruiting the PIC to the 5' end of the mRNA. eIF4B, eIF4H, and eIF4G together are responsible for stimulating eIF4A helicase activity which unwinds hairpin structures within the untranslated region and aids in scanning. In Giardia, the only detectable homologs of eIF4 are GleIF4A and GleIF4E2. Without its stimulating partners and with the lack of a 5' untranslated region containing secondary structures, the role of GleIF4A in translation is largely unknown in Giardia. Current literature shows a novel interaction between GleIF4A and GleIF3i. GleIF3i exists as a subcomplex with GleIF3b and GleIF3g and this subcomplex is involved in nearly every step of translation initiation. The aim of our study was to elucidate what interactions GleIF4A may have with this eIF3 subcomplex and what implications it may have in understanding GleIF4A's function utilizing both in vitro and in vivo assays.

PILOT PROJECT: 8:31 AM–8:41 AM

Protective role of Growth Hormone Releasing Hormone Antagonists in Endothelial Barrier Dysfunction

Nektarios Barabutis, Seetharama Jois
University of Louisiana Monroe

Abstract: Growth Hormone - Releasing Hormone is a hypothalamic hormone which regulates the release of Growth Hormone from the anterior pituitary gland; and has been associated with cancer-promoting activities. Growth Hormone Releasing Hormone antagonists (GHRHAnt) were developed to suppress experimental cancers both in vivo and in vitro. Recent evidence in endothelial cells suggest that GHRHAnt exert anti-inflammatory activities, reduce the generation of reactive oxygen species, and utilize the unfolded protein response (UPR) to enhance barrier function. Endothelial hyperpermeability is the hallmark of Acute Respiratory Distress Syndrome, the severe form of Acute Lung Injury (ALI). Targeted therapy for that lethal disorder does not exist. Our works utilize experimental models of LPS-induced barrier dysfunction, to study the pathogenesis of endothelial dysregulation, and contribute towards the development of new therapeutic approaches towards the corresponding disorders (e.g., sepsis, ARDS). Our research in endothelial cells suggests that GHRHAnt post-treatment counteracts LPS-induced paracellular hyperpermeability, and suppress cofilin and myosin light chain 2 activation in the inflamed cells. Moreover, GHRHAnt protect mice against LPS-induced ALI, and UPR suppression counteracts those beneficial effects. Ongoing research aims to elucidate mechanisms mediating the protective effects of GHRHAnt in LPS-induced ALI; and identify UPR-related elements mediating those events.

PILOT PROJECT: 8:42 AM–8:52 AM

Formulation and characterization of pluronic lecithin organogel as an efficient transdermal delivery vehicle of the flavonol fisetin and its potent derivatives

Anthony Walker, Jean C. Chamcheu, Khalid A. El Sayed, Tarun K. Mandal
University of Louisiana at Monroe College of Pharmacy, Xavier University of Louisiana College of Pharmacy

Abstract: The major objective of this study is to prepare topical gel formulations of fisetin, a natural dietary polyphenol and DF21, a more potent synthetic derivative of fisetin, and to characterize their efficacies as safer alternatives for treating cutaneous inflammatory disorders with an emphasis on psoriasis. Recent reports and our preliminary research findings showed that i) topical application of fisetin alleviates psoriasis-like lesions in a 3D full-thickness reconstituted human skin equivalent model of psoriasis (FTRHSP), ii) fisetin modulates chronic inflammatory conditions, and iii) a novel potent amine substituted derivative of fisetin, DF21, modulates skin cells hyperproliferatory responses (>176-fold) and over 15-fold more mTOR kinase inhibitory activity compared with fisetin in vitro. These formulations are hoped to present an advantage over others with less potential for unwanted, adverse side effects. Pluronic lecithin Organogel (PLO) is a non-pharmacologically active extemporaneous formulation that is non-toxic, non-irritating, non-allergenic and works rapidly with predictable and reproducible effects. PLO has no

pharmacological activity within the body as the skin barrier rapidly resumes to its natural state after its use, and it is cosmetically acceptable. The topical route of administration within the body and skin barrier will allow the active ingredient to effectively bypass the oral and gastrointestinal system, eliminating first pass metabolism, bridging bioavailability issues, and avoiding side effects and problems related to the gastrointestinal tract passage. Based on these positive characteristics, we posit that the medicated PLO formulations will provide successful transdermal delivery of the active ingredient across the skin and increase the active ingredient's permeation ability for systemic absorption to maximize local and systemic therapeutic effects.

PILOT PROJECT: 8:53 AM–9:03 AM

The duration of perturbations in firefighter neural function and decision-making following rapid heat stress exposure.

Cory Coehoorn, Jillian Danzy, Aaron Adams, Naina Lal, Daniel Poole, and Elizabeth Disbrow
LSU Health Shreveport, LSU - Shreveport, LSU Health Shreveport, LSU Health Shreveport, LSU Health Shreveport

Abstract: Previous research has demonstrated the short-term impact of rapid heat stress (RHS) on neural function and decision-making. Still, no research to date has evaluated the duration of the neural function and decision-making perturbations following RHS exposure. Purpose: To study the impact of RHS on neural function and decision-making pre-, immediately post-, 24-hours post-, and 48-hours post-RHS exposure. Methods: Nineteen subjects (mean 33.1 ± 9.0 years) performed a steady state exercise protocol while in firefighter personal protective equipment (PPE) in an environmental chamber. Electroencephalography (EEG) frequency band data and decision-making error rates were recorded during a Go/No-Go task pre-, immediately post-, 24-hours post-, and 48 hours post-RHS exposure. Results: Frequency band neural function data demonstrated an increase between pre- and immediately post-RHS exposure for the theta ($F(3,45) = 4.627$, $p \leq 0.01$) and delta ($F(3,45) = 7.504$, $p \leq 0.001$) waveforms. There was no difference between pre-, 24-hours post-, and 48-hours post-RHS exposure for the theta and delta frequency bands. Additionally, there was no difference between the alpha and beta frequency bands at any time. Lastly, there was an increase ($F(3,45) = 2.975$, $p \leq 0.05$) in the Go/No-Go decision-making errors between the pre-RHS and immediately post-RHS exposure trials. There was no difference between the pre-, 24-hour post-, and 48-hour post-RHS exposure trials. Conclusion: An increase in the delta frequency band is associated with the inability to think. An increase in the theta frequency band is linked to inattentiveness. Therefore, the current results support previous literature demonstrating that firefighter cognitive function is impacted post-RHS exposure immediately. The results also show a novel finding: neural function returns to baseline at 24 hours post-RHS exposure. Therefore, there do not appear to be long-term neural function deficits following an acute RHS exposure.

PILOT PROJECT: 9:04 AM–9:14 AM

A Multi-View Spatiotemporal Hierarchical Deep Fusion Learning Model for Decoding Human Brain Activity

Kazim Sekeroglu
Department of Computer Science, Southeastern Louisiana University

Abstract: This research aims to explore the decoding of human brain activities using EEG signals for Brain Computer Interfaces (BCI) by utilizing a multi-view spatiotemporal hierarchical deep learning. Decoding of motor movement and decoding of visual information from the human brain are the two most common decoding problems in BCI. In this research, we explore the decoding of visual information from human brain utilizing EEG signals. EEG data is a record of electrical activity of the brain over a period of time. EEG signals have been used in diagnostics of neurological disorders as well as in brain computer interfaces. Analysis and the recognition of EEG signals have been studied for decades. The common approach in the analysis and the classification of EEG signals is based on one-dimensional (1D) time series input commonly represented by frequency band power features and time point features. In this project, we study the recognition of EEG signals based on 3D EEG data created by transforming 1D EEG signals into 2D spatiotemporal image sequences which are explored based on the views from different planes. According to recent studies in computer vision, Deep Learning is considered the state-of-the-art method for image recognition, and our previous studies have shown that hierarchical deep learning improves the recognition accuracy further. Therefore, we explore the use of multi-view hierarchical deep learning methods for the classification of 2D spatiotemporal image sequences. In addition, the Recurrent Neural Networks have been known for their great performances in the prediction and classification of the time series data. Thus, in the proposed hierarchical learning scheme, we explore the use of Convolutional Neural Network (CNN) with Long-Short Term Memory (LSTM) within the proposed hierarchical learning scheme.

TRANSLATIONAL PROJECT: 9:15 AM–9:25 AM

Preclinical Development of Small Molecule Therapeutics for Alzheimer's Disease

Santosh D'Mello, Dylan Roberts, Hailey Brokenberry, and Xiaohong Lu
LSU Shreveport, LSU Health Shreveport

Abstract: Neurodegenerative diseases have a devastating effect on the quality of life of patients afflicted with them and have a major economic impact on society. The most prevalent of neurodegenerative disease is Alzheimer's disease (AD), which affects more than 50 million people worldwide. AD is characterized by progressive cognitive impairment starting with a decline in memory, resulting from selective loss of neurons in the hippocampus and cortex. There is currently no treatment that can stop or slow down the relentless loss of neurons in AD. Several years ago, my lab discovered that a commercially available compound of the 3'-indolone class and sold as an inhibitor of c-Raf, was highly neuroprotective in cell culture as well as animal models of neurodegenerative disease. Starting with GW5074 we identified several other 3'-substituted indolones that were also neuroprotective, but that appeared to work through mechanisms different from GW5074. The paradigm we used to evaluated neuroprotection by these compounds was cultured cerebellar granule neurons (CGNs) switched from depolarizing medium to non-depolarizing medium. While an excellent in vitro model to study activity-dependent regulation of neuronal survival during development, the CGN model has limited relevance to age-associated neurodegenerative diseases like AD. As a step towards identifying neuroprotective compounds for the treatment of Alzheimer's disease, we are using the HT22 cells, a mouse hippocampally-derived cell line, to identify compounds of the 3'substituted indolones and 1,4 benzoxazines classes that have neuroprotective activity. During the funding period we developed a paradigm in which HT22 are treated with glutamate at increasing doses. We have so far tested three commercially-available 3' substituted indolone compounds (GW5074, a c-Raf inhibitor, SU6656, a Src inhibitor, and PKR

inhibitor) and one 1,4 benzoxazine (NGN-006) in this paradigm. While GW5074 is partially protective against glutamate-induced toxicity, the other three compounds were highly protective. We are currently beginning studies to test these three compounds in Drosophila models of neurodegenerative disease.

FULL PROJECT: 10:00 AM–10:25 AM

Nanoparticulate Magnetic Imaging Agents for Cancer Diagnostics

Vladimir Kolesnichenko, Jonathon Q. Brown, Galina Goloverda and Thomas Wiese
Tulane Biomedical Engineering; Xavier University

Abstract: Cancer diagnostics remains one of major challenges of biomedical science. One of the most promising approaches relies on using an imaging agent which can recognize and bind to the cancerous cells, and then be detected by optical or MRI imaging. Ultrasmall magnetic nanoparticles are very attractive candidates for such an imaging agent development because they can be easily detected by MRI or MPI, and also because they can be constructed using stable and relatively non-toxic materials. In this project we will develop new imaging agents which can be selectively recognized by cancerous cells. These agents will be composed of our "home-made" individual 3-5 nm magnetic iron oxide particles coated with covalently bound organic oligomers of an optimal size, so that overall size of the nanoparticulate adduct will not exceed 15-20 nm. The organic coating for these particles (linker molecules) is our own recently developed composition consisting of 2-hydroxyisophtalate (tenacate) coordinating head and an amphiphilic spacer composed of a variable-length ethylene oxide units. These linkers will be conjugated at their termini with biomolecules responsible for the cell specificity (vectors). In our imaging agent, the length and structure of the linker molecules will be adjusted for optimal pharmacokinetic properties. We will perform in vitro studies in uMUC1-positive and negative cell lines to assess specificity, cellular uptake, cellular distribution and toxicity of the nanoparticles, as a function of the organic shell structure and size. Our hypothesis is that targeted superparamagnetic nanoparticles of an average size of 15-20 nm will have a high level of specific binding to uMUC-1 antigen on the surface of cancer cells, but a reduced level of nonspecific binding to blood serum proteins. Therefore they will have a chance to avoid phagocytic clearance as well as early renal clearance and become an effective tool for early detection of cancer.

FULL PROJECT: 10:40 AM–11:05 AM

micro-RNA therapy against cell cycle progression for Lung Cancer treatment

George Matthaiolampakis, Karen Briski, and Konstantin Kousoulas
University of Louisiana at Monroe, LSU School of Veterinary Medicine

Abstract: Lung cancer (LC) is the leading cause of cancer-related deaths in the US. Cell cycle regulation is a promising approach for cancer treatment and has translated to patient care. Yet, such treatments hae not yet found applicability towards LC patient treatment. Nucleic acid-based therapeutics has become to prominence for use in many diseases, including cancer treatment. micro-RNAs (miRNAs) are natural short nucleic acids capable of regulating gene expression. We focused on two miRs, miR-143 and miR-506, that their transient tranfection regulates CDK1 and CDK4/6, respectively. To evaluate the long-term effects of the two miRs, we developed stable deregulations of the miRs in A549 cells, individually or in combination. Using fluorescence activated cell sorting (FACS), we collected the highest GFP-fluorescence expressing cells and

confirmed the miR deregulation using quantitative real-time polymerase chain reaction (qRT - PCR), as well as performed cell cycle analysis using Flow cytometry. TaqMan qPCR showed over five-fold increase of the basal expression for the respective miRs for the stable upregulation groups, and a respective approximately >50% downregulation of the two genes for the stable downregulation groups. Our results support that the miR combination upregulation induces a G2 arrest in opposition to the respective downregulations, while the deregulation of the individual miRs were demonstrating a complex, undefined behavior.

FULL PROJECT: 11:10 AM–11:35 AM

Design, Synthesis and Evaluation of Pyrazole Derivatives as Potential Anti-Cancer Agents

Siva Murru, Seetharama Jois, Jayalaxmi Sridhar, Jean-Christopher Chamcheu
University of Louisiana at Monroe, Xavier University of Louisiana

Abstract: Cancer is characterized by the uncontrolled growth and proliferation of abnormal cells and is the second leading cause of morbidity and mortality in the world. Cancer therapy is a challenging area for medicinal chemists, in which they need to discover safe and effective chemotherapeutic agents for inhibiting cancer cell growth by interacting with specific molecular targets resulting in significant damage to the cancerous cells selectively. Consequently, much effort has been put into finding robust inhibitors that are more selective, less toxic, and less susceptible to drug resistance. Nitrogen heterocyclic compounds are an integral part of a huge number of natural and synthetic compounds and are the most important active pharmaceutical scaffolds. Among those, pyrazole derivatives can be fine-tuned to achieve desired electronic and steric effects that are essential features required for the desired biological activity. Currently we are working on design, synthesis and anticancer activity evaluation of pyrazole based small molecules. We have synthesized a library of pyrazole derivatives and tested the in-vitro antiproliferative activity against a set of lung (A549, NCI H522) and skin (GFP-A375, SKMEL-28, GFP-A431 and SCC-12) cancer cell lines. We have identified a few compounds with good potency and higher selectivity against tested cancer cell lines compared to non-cancerous cells. Based on the structure activity relationships (SARs) of the tested compounds, we have designed a library of compounds by combining/merging active pharmacophores. By developing new synthetic approaches, we have synthesized >40 compounds with the main goal of improving potency and selectivity index. In addition to that, we have performed several mechanistic studies to identify affected biological pathway/target(s) from the drug treatment. From collaborative efforts, we have recently obtained useful data from ProliFiler-MoA studies and RNA Seq-pathway analysis as part of mechanistic studies.

FULL PROJECT: 11:40 AM–12:05 PM

Life in the fast lane: Testing for congruence among transcriptomic signatures

Kyle Piller, and Brant Faircloth
Southeastern Louisiana University

Abstract: Traditionally, species are developed as model organisms because they possess interesting life-history features or unique genetic attributes/physiologies that make them amenable to laboratory studies and experimentation. The Turquoise Killifish (Nothobranchiidae: Nothobranchius furzeri) is a recently developed model organism that is being used to investigate

the process of aging and age-related diseases. This particular species is amendable to age-related studies because it is an annual species that can complete its entire life-cycle between 10 and 31 weeks. This is interesting because annualism is a relatively rare life-history trait among vertebrates. Within the Nothobranchiidae, three life-history patterns exist including annualism, non-annualism, and semi-annualism. These life-history differences offer the unique opportunity to examine differences in gene expression patterns across these life-histories. To examine differences, QuantSeq data was gathered from liver tissue from multiple species of killifishes, spanning all three life-histories, to compare gene expression patterns. For the 500 most variable genes, the results indicate that comparisons involving annual species have the highest number of differentially expressed genes (DEGs) with the greatest number of DEGs between annuals and non-annuals, and the smallest number of differences between semi-annual and non-annual species. In addition, differential expression patterns for DNA repair genes also were examined. The same patterns were recovered when analyses were limited to DNA repair genes. The implications of these results and the future direction of this study will be discussed.

FULL PROJECT: 1:05 PM–1:30 PM

Multifunctional Living Stem Cell-Laden Hydrogel Networks for Directed Tissue Regeneration

Mary Caldorera-Moore, and Chris Kevil
Louisiana Tech University, LSU Health Shreveport

Abstract: Parallel advances in stem cell technologies and in biologically mimicking (biomimetic) material constructs can enable the restoration and direct replacement of diseased cells and tissues. One area of particular interest is the regeneration of tissue for the treatment of chronic wounds. Chronic wounds affect 6.5 million people in the USA with over 25 billion USD annually in health care costs. Current treatment options include standard moist dressings, bioactive dressings, scaffolds, protease modulating ointment, and iodine loaded matrix. Most of these treatments tend to have a singular function; antibacterial, absorption, or pH regulation and they only treat the side effects of the wound not the cause. Though effective when used alone, these treatments often require a combination of different treatment options to provide effective patient care. Low patient compliance, increased need for wound maintenance, and increased care cost has increased the need for a low maintenance multifunctional treatment option. The long-term goal of this research project (now funded through a LBRN full grant 2022-2025) is to create a proactive biomaterial capable to address these limitations. To accomplish this, I hypothesize that a responsive biomaterial scaffold with stem cells will create a proactive wound dressing for improving the healing and re-epithelization rates in chronic wounds. Previously our lab has developed responsive hydrogel biomaterial composed of antimicrobial, mucoadhesive, and hemostatic chitosan-genipin. These hydrogels can serve as a scaffold for stem cells, which have previously been shown to significantly reduce wound size and wounds healing rate when injected into the wound area.

FULL PROJECT: 1:35 PM–2:00 PM

Development of fisetin as a novel inhibitor co-targeting PI3K/AKT/mTOR/Rac1 and IL-17A for Treating Psoriasis

Jean Christopher Chamcheu, Samuel T. Boateng, Tithi Roy, Sergette Banang-Mbeumi Emmanuelle M. Ruiz, Roxane-C N. Chamcheu, Anthony Walker, Kousoulas G. Kousoulas, and Shile Huang
University of Louisiana at Monroe, LSU School of Veterinary Medicine, LSU Health Shreveport

Abstract: Psoriasis is a common and currently incurable inflammatory skin disorder characterized by aberrant immune mediators-induced skin hyperplasia, infiltratory immune cells, upregulated Akt/mTOR pathway and dysregulated psoriatic lesions skin barrier. Several drugs that target Th1/Th17 cytokines or their receptors have been approved for treating psoriasis in humans with variable results necessitating improved therapies. Fisetin is a natural dietary ingredient that has shown anti-oxidant and anti-proliferative properties and covalently binds mTOR/S6K1. Fisetin's effects on psoriasis-like features and its underlying mechanisms is not been clearly defined, and we herein address these. Fisetin's immunomodulatory effects on Th1/Th17-cytokine-activated adult human epidermal keratinocytes (HEKa) and anti-CD3/CD28-stimulated inflammatory CD4+ T cells was examined and compared with a known mTOR inhibitor, rapamycin in vitro. Transcriptomic analysis of HEKa revealed functional enrichments of genes related to PI3K/Akt/mTOR and autophagy pathways, psoriasis, and epidermal development. Using in silico molecular modeling, we observed a high and preferential binding affinity of fisetin to IL-17A when compared to its receptor. In vitro, fisetin markedly suppressed mTOR activity, promoted the expression of autophagy markers and curbed the increased IL-17A secretion elicited by activated CD4+ T lymphocytes or T lymphocytes co-cultured with HEKa. Preclinically, topically applied fisetin significantly ameliorated imiquimod (IMQ)-induced psoriasis-like inflammation in C57BL/6J mice by suppressing proliferation, inflammation and phosphorylation of Akt/mTOR, while inducing keratinocyte differentiation and autophagy. Taken together, our observations suggest that fisetin can be a potential therapeutic molecule to be developed for the management of psoriasis and possibly other inflammatory skin diseases.

FULL PROJECT: 2:05 PM–2:30 PM

Elucidation of Plant-Derived Anticancer Alkaloid Biosynthetic Pathways: Prospects of Enzyme Engineering for Diversification of Natural Products

Vonny Salim, Audrey Lashley, Sara-Alexis Jarecki, Jessica Kading, Michael Minamyer, Ryan Miller, Paul Erba, Stephanie Provenzano, Keelin North, Elahe Mahdavian, Urska Cvek, and Shile Huang
LSU Shreveport, LSU Health New Orleans, LSU Health Shreveport

Abstract: Medicinal plant species, such as Catharanthus roseus, Rauwolfia serpentina, and Camptotheca acuminata produce a class of plant specialized metabolites, known as monoterpene indole alkaloids (MIAs). Two of these species are valuable producers of chemotherapeutic agents, namely vinblastine from C. roseus and camptothecin from C. acuminata. Despite their wide applications, these compounds are still isolated and purified from plants with low yields. Recently, synthetic biology and next generation sequencing technologies have accelerated the identification of MIA biosynthetic enzymes of C. roseus to allow the reconstitution of plant vinblastine pathways into microbial systems. While the upstream parts of MIA pathways up to the synthesis of central intermediate strictosidine have been elucidated, the remaining downstream enzymes involved in camptothecin biosynthesis remain to be functionally characterized. Previously, several candidate genes involved in camptothecin pathways have been identified by utilizing transcriptomics,

genomics, and metabolomics tools. The complexities of camptothecin pathway in C. acuminata with the involvement of multiple isomeric intermediates are matched by the findings of several homologous genes driven by tandem duplications within its genome. Here, we highlight the significance of structural comparative analyses to validate the biochemical characterization of these proteins, such as the enzyme forming the central intermediate in MIA pathway (strictosidine synthase), glucosidases, and methyltransferases. Further insights of their substrate binding pocket, dimerization, and catalytic amino acid residues modulating their substrate specificities, regioselectivities, and mechanisms will facilitate the development of enzyme engineering. We expect that these efforts will improve the production of MIAs and diversification of plant alkaloids with enhanced medicinal properties.

FULL PROJECT: 2:35 PM–3:00 PM

MindPrint: Exploring uniqueness of individuals' brain signals

Omer Soysal
Department of Computer Science, Southeastern Louisiana University

Abstract: This research aims to accomplish 1) developing a system to explore characteristics of individuals' brain signals and 2) developing a curriculum to train the workforce for computational aspects of brain signals. The brain state of a specific population will be explored under daily naturalistic stress; collected anonymized data will be shared with researchers to support brain initiative research. In addition, the PI's proposed protocol will help to explore the effect of stimuli on the permanence and distinctiveness of mind-print of individuals' brain. Another novel approach to be explored in this research is developing an algorithm for searching possible patterns in an intelligent way by means of a data mining technique. Note that the proposed framework utilizes a hypercube in representation of the brain activity despite other approaches that separate channels and/or brain wave bands to create input features or feature maps. Furthermore, developing and implementing a curriculum to train the workforce in computational biomedical applications utilizing brain signals is new in the region. This curriculum can also be transferred to workforce training programs nationwide.

Poster Session Abstracts

Friday, January 20th
Even Numbers 4:00 PM – 5:00 PM
Odd Numbers 5:00 PM – 6:00 PM

1. The duration of perturbations in firefighter neural function and decision-making following rapid heat stress exposure. Jillian Danzy, **Aaron Adams**, Naina Lal, Daniel Poole, Elizabeth Disbrow, Cory Coehoorn. LSU Health Shreveport, LSU-Shreveport, LSU Health Shreveport, LSU Health Shreveport, LSU Health Shreveport

Abstract: Previous research has demonstrated the short-term impact of rapid heat stress (RHS) on neural function and decision-making. Still, no research to date has evaluated the duration of the neural function and decision-making perturbations following RHS exposure. Purpose: To study the impact of RHS on neural function and decision-making pre-, immediately post-, 24-hours post-, and 48-hours post-RHS exposure. Methods: Nineteen subjects (mean 33.1 ± 9.0 years) performed a steady state exercise protocol while in firefighter personal protective equipment (PPE) in an environmental chamber. Electroencephalography (EEG) frequency band data and decision-making error rates were recorded during a Go/No-Go task pre-, immediately post-, 24-hours post-, and 48 hours post-RHS exposure. Results: Frequency band neural function data demonstrated an increase between pre- and immediately post-RHS exposure for the theta ($F(3,45) = 4.627$, $p \leq 0.01$) and delta ($F(3,45) = 7.504$, $p \leq 0.001$) waveforms. There was no difference between pre-, 24-hours post-, and 48-hours post-RHS exposure for the theta and delta frequency bands. Additionally, there was no difference between the alpha and beta frequency bands at any time. Lastly, there was an increase ($F(3,45) = 2.975$, $p \leq 0.05$) in the Go/No-Go decision-making errors between the pre-RHS and immediately post-RHS exposure trials. There was no difference between the pre-, 24-hour post-, and 48-hour post-RHS exposure trials. Conclusion: An increase in the delta frequency band is associated with the inability to think. An increase in the theta frequency band is linked to inattentiveness. Therefore, the current results support previous literature demonstrating that firefighter cognitive function is impacted post-RHS exposure immediately. The results also show a novel finding: neural function returns to baseline at 24 hours post-RHS exposure. Therefore, there do not appear to be long-term neural function deficits following an acute RHS exposure.

2. Design and synthesis of pyrazolone molecular hybrids as potential anticancer agents for the control of resistant colon cancer. **Siriki Atchimnaidu**, Heba Elsayed, Hassan Mohamed Lotfy Ebrahim, Khalid El Sayed, Siva Murru. Chemistry, School of Sciences, College of Arts, Education and Sciences, School of Basic Pharmaceutical Sciences, College of Pharmacy, University of Louisiana Monroe.

Abstract: Heterocyclic compounds are an integral part of a huge number of natural and synthetic compounds and play important roles in biological systems. Among those, pyrazoles and pyrazolones are very effective pharmacophores in several important biologically active molecules. Catalytic cross-coupling reactions are efficient synthetic approaches for the derivatization of pyrazolones to fabricate corresponding molecular hybrids. We have developed a microwave assisted reaction condition for C-N bond formation (Buchwald-Hartwig cross-coupling) between haloarene of the 1,3-diarylpyrazolones and the heterocyclic secondary amines such as piperidine,

pyrrolidine, and morpholine. Alternatively, we have adopted Pd-catalyzed approaches such as Heck, Suzuki and Sonogashira cross-couplings as important tools for molecular hybridization. Our current focus is on the design and synthesis of pyrazolone-molecular hybrids, and evaluating their antiproliferative activity against resistant colon cancer cell lines. Colorectal cancer (CRC) is ranked third amongst the most common cancers affecting worldwide. Additionally, development of drug-resistance by colon cancer cells leading to failure of the treatment by current anticancer drugs. Moreover, multi-drug resistance is the major drawback towards the drug-resistant colon cancer. We have synthesized a library of molecular hybrids using above mentioned cross-coupling reactions and identified two sets of potential compounds with good antiproliferative activity against drug-resistant colon cancer cell lines. Detailed experimental data from the synthetic approaches and anti-proliferative activity screening will be presented.

3. Applying the Brakes: Understanding the Role of Conformational Changes in Kinesin-5. Nelson Brown, **Justice Austin**, Kennedy Drake, Jordan Campbell, Caleb Cook, Joseph Chaney. Xavier University of Louisiana.

Abstract: Human Kinesin-5 (Eg5) is an anticancer drug target and a molecular motor protein integral to the assembly of the bipolar spindle during mitosis. The neck-linker of Kinesin-5 is a 12-15 residue segment at the N-terminus that plays an important role in the processive transport of intracellular cargo along the microtubule surface. A deeper analysis of Kinesin-5 can unlock key details and the potential of these mechanisms. Although Kinesin-5 is an important anticancer target, much work is already completed on Kinesin-1. Kinesin-1 is one of the few kinesin motor proteins with a dimeric structure documented. This information allows us to have an idea of what Kinesin-5 may look like in form and provides a method for direct comparison. The goal is to determine the effects of insertions in the neck-linker of Kinesin-5 by investigating the catalytic activity, in vitro, and microtubule motion. The insertions are performed at different positions in the neck linker to determine whether more downregulation occurs at different positions on the gene. These insertions are analyzed using ATPase assays to determine the activity of mutated proteins. Wild-type Kinesin-5 will be studied to compare the results with those of the mutated proteins. Our project seeks to give insight as to how the neck-linker controls structural asymmetry and initiation of the coil-coil domain in Kinesin-5. Our future goal is to test the response of Kinesin-5 to known Kinesin inhibitors and to generate a novel inhibitor.

4. N-Boc-hydroxylamine as a Boc-donor Agent for the Catalytic N-tert-Butoxycarbonylation. **David Basnet**, Siriki Atchimnaidu, and Siva Murru. University of Louisiana at Monroe.

Abstract: The presence of an amino group in various drug molecules and their key intermediates makes protection and deprotection of the amine functionality a necessity during their synthesis. Compared to acylation, tert-butoxycarbonylation can be deprotected under mild conditions with high purity of products. Moreover, tert-Butyl carbamates are stable in the presence of a wide range of nucleophiles and under alkaline conditions and are very liable under mildly acidic conditions to liberate the parent amine. In general, tert-butoxycarbonylation is achieved by the treatment of an amine with Boc-anhydride [(Boc)2O] in the presence of organic/inorganic bases. However, the reported methodologies have various drawbacks such as long reaction times, the requirement to prepare the tert-butoxycarbonylation reagents, the high toxicity of DMAP and its derivative. Further, the base-catalyzed reactions often lead to the formation of isocyanate urea and N,N-di-Boc derivatives. We present herein the combination of Cu(I)Cl and pyridine as a highly efficient

catalyst for the formation of tert-butyl carbamates from pyrazoles and indazoles at room temperature. We have tested a variety of heterocyclic compounds and amines and performed controlled experiments which are discussed in this poster.

5. Membrane rafts regulate autophagy process in e-cigs challenged lung epithelial cells. **Rizwana Begum**, Shilpa Thota, Nandini Bidarimath, Dhruthi Muthyala, and Sanjay Batra. Southern University and A&M College.

Abstract: Exposure to cigarettes and other nicotine-based products results in persistent inflammation in the lung. In recent years the massive popularity of electronic cigarettes (e-cigs) has become the latest trend among adults and youth alike. E-cigarette vapor-induced oxidative stress promotes protein breakdown, DNA damage, and cell death, culminating in a variety of respiratory diseases. Autophagy is essential for cellular homeostasis and adaptation to extreme conditions, however, its regulation during e-cigs induced stress is far from being clear. We recently identified that caveolin-1, a prominent constituent of caveolae rafts on the plasma membrane can regulate the autophagy process in cigarette smoke extract-challenged lung epithelial cells. In light of these facts, we hypothesized the important role of lipid rafts in regulating the autophagy process in e-cig vapor condensate (tobacco flavor; TF-ECVC±N) challenged human lung epithelial cells (A549). Our results demonstrate TF-ECVC mediated increase in-1) transcription and translation of lipid raft associated proteins (caveolin-1, caveolin-2, flotillin-1, and flotillin-2); 2) transcription of autophagy-related genes (Beclin-1, ATG12, ATG16, and LC3) in A549 cells. We also observed the localization of key autophagy proteins-ATG5, ATG12, and LC3B proteins in the lipid raft fractions isolated from TF-ECVC-challenged alveolar epithelial cells. Furthermore, using in silico approach we provide evidence of a strong interaction of ATG5 with nicotine-bound Caveolin-1 (-923 KJ/mol) compared to unbound Caveolin-1 (-710 KJ/mol). Our results provide critical information about the possible molecular mechanisms which regulate the autophagy process during ECVC exposure.

6. Role of Small Ribosomal Subunit Protein ES6 in DPE-induced autophagy/apoptosis: in vitro study. **N. Bidarimath**, D. Mutyala, S. Thota. R. Begum, and S. Batra. Laboratory of Pulmonary Immunotoxicology, Department of Environmental Toxicology Southern University and A&M College.

Abstract: There is a growing threat to our environment due to the rapid increase in the use of diesel engine motors and non-road types of equipment in the agriculture and industrial sector. Being a relatively less explored area, determining the molecular mechanisms associated with inflammation/toxicity induced by diesel particulate matter/extract (DPM/DPE) is highly warranted. Using human lung epithelial cells with type II characteristics (A549) we observed a significant increase in the pro-apoptotic markers and reduced expression of autophagy-related genes following the challenge with 25 ug/ml DPE for 48h. Specifically, we observed-a) increase in the transcription of proapoptotic genes: BAX, BAK, FADD, FAS; b) translational induction and/or activation of effector/executioner-Caspase (Casp)8 and Casp3, and inflammatory Casp1; and c) abrogated transcription of autophagy-related genes in challenged cells. Additionally, using MTS assay we observed a significant decrease in the viability of A549 cells exposed to DPE at concentrations ranging from 50 to 150 µg/ml for 48h. Earlier reports suggest that the knockdown of ribosomal proteins RPS3, RPS6, and RPL24 known for their moonlighting function inhibited cell growth or induced apoptosis in breast cancer cells. Interestingly, we observed an increase in the expression of Small Ribosomal Subunit Protein ES6 (RPS6) in DPE-challenged cells. We,

therefore, hypothesized an important role of RPS6 in DPE-mediated regulation of the apoptosis/autophagy process. Conducting antibody-mediated neutralization of RPS6, we observed- a) significant rescue of DPE-induced transcription of FAS, FADD, and CASP3; and 2) an increase in the transcription of Beclin1, ATG12, and ATG16 in DPE-challenged cells. Our findings suggest a possible role of RPS6 in the FAS/FAAD-mediated extrinsic apoptotic pathway and autophagy in DPE-challenged A549 cells. Detailed in vitro and in silico studies are in progress to elucidate the molecular mechanisms.

7. The dietary antioxidant Fisetin, improves psoriasiform dermatitis in C57BL/6J mice by co-targeting mTOR/IL-17A and autophagy pathways. **Samuel Boateng,** Tithi Roy, Sergette Banang-Mbeumi, Emmanuelle M Ruiz, Roxane-Cherille N. Chamcheu, Anthony L. Walker, Konstantin G. Kousoulas, Shile Huang, Jean Christopher Chamcheu. University of Louisiana at Monroe, Louisiana State University-Baton Rouge, Louisiana State University Health Sciences Center-Shreveport.

Abstract: Psoriasis (PS) is a difficult to treat autoimmune skin disorder that afflicts over 7.5 million US adults. It is characterized by epidermal hyperplasia, and aberrant immune response and is associated with the PI3K/Akt/mTOR pathway activation. Fisetin is a natural dietary polyphenol/ingredient with anti-oxidant and anti-proliferative properties, which covalently binds mTOR/S6K1. Herein, the immunomodulatory effects of fisetin on Th1/Th17-cytokine-activated epidermal keratinocytes (HEKa) and anti-CD3/CD28-activated inflammatory CD4+ T cells were assessed and compared with rapamycin's (an mTOR inhibitor). RNA-seq analysis of HEKa revealed 12,713 differentially expressed genes (DEGs) in the fisetin-treated group compared to 7,374 DEGs in the rapamycin-treated group, both individually compared to a cytokine-treated group. Gene ontology analysis revealed functional enrichment of components of PI3K/Akt/mTOR signaling pathways, psoriasis, and epidermal development. Using in silico molecular docking, we observed a high binding affinity of fisetin to IL-17A. In vitro, fisetin significantly inhibited mTOR activity, while increasing the expression of autophagic markers Beclin1, LC3A/B and Atg5 in HEKa and suppresses IL-17A production by activated CD4+ T cells or T cells co-cultured with HEKa. Preclinically, topical administration of fisetin in an imiquimod (IMQ)-induced C57BL6J mouse psoriasis-like model exhibited a better effect than rapamycin in improving psoriasiform dermatitis and Akt/mTOR phosphorylation as well as promoting differentiation and autophagy in mice skin lesions. Fisetin also significantly inhibited T-lymphocytes and macrophage infiltration into the skin. Overall, fisetin potently inhibits IL-17A and Akt/mTOR pathway activation, and promotes epidermal differentiation and autophagy to alleviate psoriasis-like disease in mice. Altogether, our findings suggest fisetin as a potential treatment for psoriasis and possibly other inflammatory skin diseases.

8. The Effects of Potential Therapeutic Drugs in Cell Culture Models of Parkinson's Disease. **Hailey Brokenberry**, Dylan Roberts, Autumn Sanders, and Santosh D'Mello. Louisiana State University-Shreveport.

Abstract: Parkinson's disease (PD) is the second most common neurodegenerative disease and the most common movement disorder. PD is caused by the selective degeneration of dopaminergic neurons in the substantia nigra which results in striatal dysfunction. The mechanisms underlying PD are unclear and while there are medications that can mitigate the symptoms, there is no

treatment for the relentless loss of dopaminergic neurons. Exposure to MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), which is metabolized in the brain to MPP+ causes PD in animals. Addition of MPP+ to cultures of primary dopaminergic neurons or to cell lines of dopaminergic origin results in cell death. MPP+ is a mitochondrial toxin. Another mitochondrial toxin that has been used in animal and cell culture as a model of PD is rotenone, an isoflavone that is used as a pesticide. The goal of my project is to identify small molecule compounds that can be developed as therapeutics for PD. As a first step, and as part of the LBRN Summer Project, I used the SH-SY5Y cell line and treated these with rotenone for various lengths of time and with different concentrations of rotenone ranging from 5 to 20 uM. Substantial cell death was observed when at doses of 10 uM and higher and after treatment for 24 hours. I am currently testing two different compounds that we have found to be protective in a cell culture model of Alzheimer's disease in rotenone-treated SH-SY5Y cells. I am also treating SH-SY5Y cells with MPP+ and will test the two compounds in this model of PD as well. Results of these experiments will be described in my poster at the LBRN Conference.

9. Kinesin 5 Inhibition. **Jordan, Campbell**, Caleb Cook, Nelson Brown, Kennedy Drake, Justice Austin, Joseph Chaney. Xavier University of Louisiana.

Abstract: Human Kinesin-5 is a protein that can be targeted as an anti-cancer therapeutic treatment agent because it acts as an important contributor to the relapse of the mitotic spindle during mitosis. Kinesin-5 has three different parts, but the N-terminus which connects the neck linker and aids microtubular transport is the focus. By unlocking more information about Kinesin-5, we are better able to understand how the mechanism works. Currently, we use the structure and known facts about Kinesin- 1 to gain more knowledge about Kinesin- 5 because we have found that they have many similarities which can be used in further development of the anticancer target. Synthesizing of inhibitors will play an integral role in the development of the target can cells because it ceases the catalytic process when it binds. The overarching ideal of an inhibitor is a molecule that binds to an enzyme which leads to decreased activity in the reaction. The overall goal of this project is to successfully synthesize the known inhibitors Monastrol and STLC. Upon successful completion of this task, novel inhibitors will be created to target Kinesin-5 to increase therapeutic outcomes.

10. Automatic segmentation of brain tumor - comparison of few recent methods. **Subhajit Chakrabarty**, Karen Stokes, Shashank Shekhar, Luis Pena Marquez. LSU Health Shreveport, UMMC Jackson.

Abstract: Brain tumors are among the deadliest types of cancer. They are, in general, challenging to diagnose, hard to treat and inherently resistant to conventional therapy because of the challenges in delivering drugs to the brain, as well as the inherent high heterogeneity of these tumors in their radiographic, morphologic, and molecular landscapes. Brain tumor segmentation remains a challenge in medical image segmentation tasks. The objective of this work is to accurately and automatically segment intrinsically heterogeneous (in appearance, shape, and histology) brain tumors. Our dataset is BraTS, comprising 3D MRI data, that is freely available. Our methods are U-Net and Vision Transformer. U-Net is a convolutional neural network that was developed for biomedical image segmentation. It consists of a contracting path and an expansive path. Transformer, which can benefit from global (long-range) information modeling using self-attention mechanisms, has been successful in natural language processing and image classification. Many variants of the methods are available but we use the basic versions. Results indicated that

Transformer outperformed U-Net, by-and-large. This indicates that long-range modeling may be useful in this domain.

11. Improving the solubility and conformational isomerism of a grafted peptidomimetic that inhibits CD2:CD58 interaction. **Arpan Chowdhury,** Ted Gauthier, Seetharama D. Jois. School of Basic Pharmaceutical and Toxicological Sciences, College of Pharmacy, University of Louisiana Monroe, Agriculture Chemistry Department, Louisiana State University.

Abstract: Protein-protein Interaction (PPI) has been the most sought out druggable target in recent years. Our research focuses on the abrogation of these PPIs using inhibitors designed using grafted peptides, Sunflower Trypsin Inhibitors (SFTI). This research aimed at the inhibition of PPIs of co-stimulatory molecules such as CD2:CD58 interaction which plays a pivotal role in Rheumatoid Arthritis. The immune response results from complex network of signaling involving numerous PPIs. MHC of APCs presents the antigenic epitope of T-Cell Receptor of T-cells to generate immune response, which depends on other co-stimulatory molecules. The CD58/LFA3 present on APC acts as a ligand for CD2 present on T-cells, which binds to CD58 via extracellular domain, resulting in generation of inflammatory cytokines. Hence, the CD2:CD58 nexus became an important target for therapeutic intervention. CD2 binding epitope region was grafted on SFTI template to inhibit CD2:CD58 PPI, resulting in SFTI-DBF (Dibenzofuran moiety). In this peptide, Pro-Pro sequence was replaced with DBF functional group to induce the β turn in the peptide structure and to lock the conformation to one major conformation in solution. However, SFTI-DBF peptide was partially soluble in water/buffer, but completely soluble in DMSO. To circumvent the solubility issue with locked conformation, two Tyrosine analogues, namely 2,6-dimethyl and guanido groups were introduced instead of DBF in the anticipation of increasing its solubility. Cell adhesion inhibition assay was performed to evaluate the inhibitory activity of these peptides and surface plasmon resonance (SPR) find the binding affinity of peptides to CD58 protein. Circular dichroism (CD) spectroscopy was performed to verify the change in the secondary structure of the peptidomimetics designed. Solubility and conformational changes of analogs of SFTI-DBF will be discussed in relation to its ability to inhibit PPI of CD2-CD58 interactions.

12. Hitting the Brakes: Understanding the Role of Conformational Changes in Kinesin-5. **Caleb Cook**, Jordan Campbell, Nelson Brown, Joseph Chaney, Justice Austin, Kennedy Drake, Amaya Sanders, Micquel Downs. Xavier University of Louisiana.

Abstract: Human Kinesin-5 (Eg5) is a motor protein that is an anticancer drug target as a result of its importance during mitosis. During mitosis, it is responsible for guiding the mitotic spindles towards their target location and studies that have inhibited the protein led to human cells undergoing mitotic arrest, unable to perform mitosis. An important region of study within Kinsein-5 is the 12-15 residue segment called the neck-linker region. If it is possible to safely inhibit Kinesin-5, it may become possible to create more focused and safe anticancer drugs because of cancer's reliance on mitosis. However, we do not fully understand the mechanisms behind the conformational changes of the Kinesin-5. As a result, we can make use of our much deeper understanding of Kinesin-1 as more information on it is documented in the Protein Data Bank compared to Kinesin-5. Kinesin-1 is our only and best model to compare with Kinesin-5 as both proteins share conserved residues, especially in the neck-linker region. By using this information,

we can create point mutations in the neck-linker of Kinesin-5 and monitor the effect on the protein's activity. We make use of E. Coli cultures in order to replicate many copies of the mutated protein. The mutations are designed to be at shared conserved residues between the neck-linker region of Kinesin-1 and Kinesin-5 in order to compare how the changes in structure effect the ability of the proteins to make conformational changes to perform their function. If it is possible to better understand the role of specific residues have in the function of Kinesin-5, it may be possible to create more efficient anticancer drugs.

13. Exploring Disparities in Breast Cancer Treatment Outcomes. **Urska Cvek**, Phillip Kilgore, Eric Clifford, Marjan Trutschl, Tingting Li, Lauren S. Maniscalco, Deniz Gungor, Jane Gulick Sugar, Terry C. Lairmore. LSUS (Department of Computer Science), LSUHSC-S (Surgery/Oncology and School of Medicine), LSUHSC-NO (Louisiana Tumor Registry)

Abstract: Breast cancer is the most common cancer diagnosed among US women (excluding skin cancers) and is the second leading cause of cancer death among women. Disparities in cancer treatment and outcomes due to geographic and other socioeconomic variables are an increasingly recognized problem. We wanted to determine if distance to treatment facility has an effect on treatment modality and examine which socioeconomic variables have the greatest effect on measurable outcomes (i.e., breast cancer incidence, survival). We obtained the SEER Medicare database for 19 US areas for more than 700,000 breast cancer cases covering the period of 1975-2017 and performed in-depth analytics. We modeled the effect of distance between the patient's residence and the primary treatment center for more than 42,000 Louisiana breast cancer patients obtained from the Louisiana Tumor Registry database for the period of 2009-19. In Louisiana, we found significant differences in both the distance to the closest utilized facility ($p << 0.001$) and in treatment modality ($p << 0.001$) with respect to urban or rural status at the time of encounter. Significant differences were also noted in patient comorbidities, tumor size, race, and ethnicity for both treatment modality and urban residence (in many cases, $p << 0.001$). Nationally, we discovered that travel distance was influenced by demographic factors, such as socioeconomic status and urbanicity. Greater distance to treatment facility was significantly associated with both mastectomy and rural residence, respectively. Several demographic variables were also significantly associated with treatment disparity, including race and ethnicity. We identified a significant disparity in treatment of African American Medicare patients who tend to be diagnosed at a later stage, more frequently experience delayed treatment to 180 days or beyond and have a significantly greater mortality. These disparities likely represent barriers to care for subsets of patients.

14. Microwave-Assisted Catalytic C-C and C-N Bond Formation: Synthesis of Pyrazolone Molecular Hybrids. **Sabina Dahal**, Siva Murru, Atchimnaidu Siriki. Chemistry, School of Sciences, College of Arts, Education and Sciences, University of Louisiana Monroe.

Abstract: Transition-metal-catalyzed cross-coupling reactions have become essential tools for the preparation of wide range of natural and synthetic bioactive compounds These catalytic reactions serve as important tools for carbon-carbon (C-C) and carbon-heteroatom (C-N / C-O) bond formations in the synthesis of pharmaceuticals and other useful molecules. Cross-coupling reactions have played a critical role enabling the rapid expansion of structure-activity relationships (SAR) during the drug discovery phase to identify a potent candidate and facilitate subsequent

drug development processes. Despite these attractive synthetic properties, continuous development of these coupling reactions has been the focus of ongoing efforts in order to improve the selectivity, efficiency and sustainability. . Our focus has been on creating diverse molecular hybrids via microwave-assisted Pd-catalyzed C-C and C-N bond formation reactions. To achieve this, we have optimized the reaction conditions, such as solvent, microwave power, and reaction time. The reactions include coupling halo-aryl pyrazolone substrates with various organometallic nucleophiles, and as a result, they belong to a family of C-C cross-coupling reactions. Because of their stability, simplicity in preparation, and low toxicity, boronic acids are frequently utilized in cross-coupling reactions. Another interesting coupling approach for making pyrazolone molecular hybrids is the formation of a C-N bond between the halo-aryl pyrazolones and the secondary amines (piperidine, pyrrolidine, morpholine etc.) using Pd-catalyzed coupling reactions. We have designed and synthesized a series of coupling products of pyrazolones through C-C and C-N bond formation reactions. We will present the details of reaction optimizations, structures of synthesized pyrazolone molecular hybrids and the anticancer activity data of selected compounds.

15. Optimizing features selection to improve VGG19 Accuracy in White Blood Cell Classification. **Prabhat Dhungana**, Qingsong Zhao. Louisiana State University Shreveport.

Abstract: When abnormal number of leukocytes are produced in the bone marrow, symptoms like bleeding, fatigue and infections occurs that causes White Blood Cell (WBC) Leukemia. The detection of the cancer-causing cell is important. The main objective of this study is to effectively classify the white blood cell leukemia through a series of Transfer Learning using state of art VGG19 model and statistically enhanced salp algorithm (SESSA). We use pre-trained CNN models with transfer learning in the WBC Images and extracted features from VGG19 model. The extracted features are then passed thorough the SESSA features for future selection, then we applied the proposed method in the WBC Leukemia datasets for effective classification. We observed better accuracy after the SESSA selected 500 features out of 25k features extracted through VGG199 model. The proposed optimization algorithm is evaluated using six classifier algorithms (SVM, Decision Tree, KNN, Naïve Baye, Adaboost and MLP) using accuracy, F1, Specificity and sensitivity metrics with average performances Accuracy of 92%. The performance of the proposed method on the image dataset shows that only the most relevant features are selected by the algorithm for effective classification of WBC Leukemia with small future numbers with reducing computational time and resources. The higher accuracy obtained thorough the proposed method shows that it can be applied to more complex classification problems, saving time and resources with better performances.

16. Development of green methods for the synthesis of drug scaffolds. **Brooke Diehl**, Jumanah Hamdi, Janelle Do, Loandi Cruz, Mark L. Trudell. University of New Orleans.

Abstract: The copper catalyzed click [3+2] cycloaddition of alkynes with azides has become a widely used and reliable synthetic method for the construction of 1,2,3-triazoles. These important heterocycles are often privileged structures and bioisosteres in a variety of medicinal chemistry applications. More recently, 1,2,3-triazoles have also found application in various areas of agricultural chemistry and polymer chemistry. Early examples of copper catalyzed click [3+2] cycloaddition of alkynes with azides used a variety of copper salts under homogenous conditions. While these methods were quite effective and high yielding, soluble copper made recovery of the

catalyst difficult and produced products contaminated with undesirable levels of copper metal. To address this issue, attention has focused upon the development of heterogeneous systems with copper immobilized on a variety of solid supports. These strategies include copper salts immobilized via ligand coordination to chemically modified solid surfaces like silica gel, alumina and various polymers. The kaolinite-related clay, halloysite (Hal), has been identified as a solid support for numerous chemical applications. The morphology of Hal particles is highly diverse, but the most common shapes are elongated, curled particles that form nanotubes or nanoscrolls. Hal nanoscrolls are generally 0.2-2 μm in length, having an inner diameter size of 10-40 nm and an outer diameter size of 40-70 nm. We have recently shown that transition metal nanoparticles encapsulated in halloysite afford highly reactive catalytic systems for organic transformations in aqueous media. We have prepared and characterized a nanocomposite of CuNP encapsulated in halloysite (Cu@Hal). Preliminary studies have shown Cu@Hal to possess remarkable catalytic activity for the click [3+2] cycloaddition reaction. The proposed project will be to evaluate the scope and limitations of Cu@Hal for the synthesis of 1,2,3-triazole drug scaffolds.

17. Does D-Cysteine Inhibit Bacillus anthracis spore-associated Alanine Racemase (Alr)? **Samuel Donn**, Rebecca Giorno-McConnel. Louisiana Tech University.

Abstract: Background: *Bacillus anthracis* spores are dormant infectious particles. Under the right conditions, these particles germinate and transition into their dangerous and active form (anthrax). Spores are notoriously resistant to harsh, usually sterilizing conditions; and can stay dormant on a surface for years. Spore germination (leaving dormancy) begins whenever the correct nutrients are present (typically L-alanine and an amino acid or nucleoside). Alanine racemase (Alr) converts L-alanine (germinant) to D-alanine (germination inhibitor) and vice versa, affecting the germination rates of spores. Alanine racemase is present in the spore coat (underneath) as well as the exosporium (outermost) layers of a B. anthracis spore. Inhibiting Alr in the presence of germinants enhances the number of spores that germinate. This in turn could enhance B. anthracis decontamination strategies, as germinated spores are more susceptible to standard inactivation techniques. Previous studies indicate that D-cysteine inhibits Alr activity in *Bacillus cereus* spores. We are exploring the possibility that D-cysteine will also inhibit Alr in B. anthracis and enhance germination. Methods: We used two different methods to determine the effect of D-cysteine on B. anthracis spores. The first was a fluorescence-based assay to measure the Alr activity of the spores. The second was a germination assay to see if D-cysteine enhanced germination. Results: We have confirmed that the fluorescence assay is not negatively affected by the D-cysteine and are currently in the process of measuring Alr activity in the presence of D-cysteine. Once complete we will conduct germination assays. We will present our findings. Conclusions: Identification of non-antibiotic Alr inhibitors such as D-cysteine may prove to be valuable for future therapeutics for anthrax infections as well as contribute to our long-term goal of developing novel strategies for wide-area decontamination.

19. Potent Antiproliferative and Proapoptotic Effects of Bioguided Fractions of Garcinia Kola Nuts in Melanoma and Nonmelanoma Skin Cancers. **JT Folahan**, ST Boateng, T Roy1, H. Li, S Banang-Mbuemi, MA Mahmud, RK Yadav, RC Chamcheu, FA Attah, H Ma, OE Olorundare, JC

Chamcheu. Univ. of Louisiana Monroe, Univ. of Rhode Island, and Univ. of Ilorin, Nigeria.

Abstract: Melanoma and non-melanoma skin cancer (NMSC) are the most common cancers in the United States. NMSC account for 5.4 million diagnosed cases annually, whereas melanoma, the more aggressive form accounts for over 80% of skin cancer-related deaths, is associated with adverse effects and/or resistance to existing treatment regimens, as major drawbacks in skin-cancer management. Therefore, new chemopreventive- and- therapeutic strategies are required to curb the incidence and mortality. Natural products are reliable sources of potentially safe and effective therapeutic agents. Garcinia Kola is a phenolic-rich herb grown in west Africa. The nut, commonly called Bitter Kola, is eaten recreationally, and used as traditional medicine for several diseases, including hepatoprotective, bronchodilating, antidiabetic, and antioxidant activities. G. kola nut extracts major phytochemical constituents include prenylated benzophenones, xanthone, biflavonoids, and kolaviron. However, G. kola's anti-cancer properties are currently under-explored. In this study, three melanoma (A375, SK-Mel-28, and B16F10), three NMSC (A431, SCC12-12, and UW-BCC1), and a normal (HaCaT-Keratinocytes) cell-lines were treated with 100-400ug of G. Kola nut methanolic extract (MeOH), N-hexane faction (Hex), aqueous fraction (AQS), ethyl acetate fraction (EtoAc), and EtoAc sub-fractions F1-3 to evaluate their effects on proliferation, cell cycle, cell motility, clonogenic potential, and apoptosis. MeOH, Hex, F2, and F3 treatments resulted in (i) a significant dose-dependent decrease in cell growth, viability, motility, and colony formation, (ii) decreased expression of cyclin D and E, indicating cell cycle arrest at the G1 phase (iii) increased expression of apoptotic markers, suggesting an induction of apoptosis in cancer cells compared to normal cells. These data strongly suggest G. Kola nut extracts as potent anti-proliferative agent that can further be explored for Melanoma and NMSC management.

20. Expression of GAD Isoforms in the Adult Mouse Olfactory Epithelium.

Kylie Francis, Jeremiah Vance Kylie White, Kathryn A. Hamilton, and Stephanie L. Villalba. LSU-Shreveport and LSU Health-Shreveport.

Abstract: During the development of cortical neurons, the neurotransmitter GABA influences the migration of the neurons and their formation of functional synapses, activity of which deters apoptosis. In the olfactory system, synaptic activity also appears to be required for survival of olfactory sensory neurons (OSNs), which are located in the olfactory epithelium. The OSNs, unlike cortical neurons, can be generated throughout life, by progenitor cells lying deep within the OE. It therefore seems reasonable that, due to its lifelong regenerative capacity, the adult OE might express glutamic acid decarboxylase (GAD), the synthetic enzyme responsible for synthesizing GABA from L-glutamic acid. For this project, we propose to use transgenic GAD65-GFP mice, in which the promoter for the 65 kDa isoform of the glutamic acid decarboxylase (GAD) gene drives expression of eGFP. These mice have been used to study GFP+ inhibitory interneurons located throughout the central nervous system, but the adult MOE has not been carefully studied. Our preliminary results show that the OE of GAD65-GFP mice contains GFP+ OSNs that are immature. The results further show that the OE expresses mRNA for both isoforms of GAD, GAD65 and GAD67. Expression of GAD65, GAD67, and GABA by the GFP+ OSNs and/or their progenitor cells would suggest that GABA plays a role, e.g., in turnover of the OSNs, axonal outgrowth, and/or formation of new synapses in the olfactory bulb.

21. Digital PCR validation of Differentially Expressed DNA Repair Genes in Killifishes. **Annalea Giamalva**, Kyle R. Piller. Southeastern Louisiana University.

Abstract: The Turquoise Killifish (Nothobranchius furzeri, Nothobranchidae) is an annual species that can complete its life-cycle between 10 and 31 weeks, making it a viable model for the study of aging and age-related diseases. Our lab is examining differential gene expression patterns across nothobranchid (Cyprinodontiformes) fishes across different life-histories including annuals, non-annuals, and facultative annuals. Results from an on-going transcriptomic analysis (QuantSeq) of these same specimens indicate large numbers of DEGs of DNA repair genes across life-histories. We have developed primers and are in the process of testing multiple primer pairs for digital PCR to validate a subset of these differentially expressed DNA repair genes. We will be comparing results to determine if there is a correlation between the QuantSeq and digital PCR results. Genes identified as showing higher levels of expression relative to other non-annual species suggests that they are likely to be relevant to the aging process and can be used in future experimental studies to better understand the genetic architecture of the aging process. At present, we are focusing on POLM-DNA, XRCC3, XRCC5. XRCC6, and several others.

22. Lipid nanoparticle formulation optimization for RNA delivery. **Md Anamul Haque**, Archana Shrestha, George Mattheolabakis. School of Basic Pharmaceutical and Toxicological Sciences, College of Pharmacy, University of Louisiana at Monroe.

Abstract: Unfavorable physiological factors at the gastrointestinal tract make oral delivery of nucleic acids challenging. The acidic gastric environment and strong enzymatic activity in the intestines promote rapid nucleic acid degradation. Lipid nanoparticles (LNPs) have recently emerged as promising nucleic acid carriers with potent transfection capacity and stability in vivo. Their potential can be appreciated by the numerous clinical trials that take place, and their recent translation to patient treatment in the COVID-19 vaccine. Unfortunately, their oral delivery is also challenging and the selection of proper lipid combinations and their respective ratios to the mRNA needs to be optimized. Our goal is to optimize LNP formulation to achieve mRNA encapsulation, stability and potent transfection, by adjusting lipid content and nucleic acid:lipid ratio. Eventually, the optimized formulation will be used for entrapment in pH sensitive nano/microcapsules for oral delivery in order to be directly released into the intestinal environment. We prepared LNPs using the DLin-MC3-DMA ionizable lipid, cholesterol, and either DSPC or DOPC, and DSG-PEG or DMG-PEG. By changing the different lipid contents, their ratios, and the nucleic acid amount, we sought to identify their optimal characteristics (i.e., size, zeta potential) and transfection signal. We utilized reference plasmid and mRNA, both expressing the luciferase gene for easy identification. Our analysis indicates the particle size of the LNPs was ~120 nm, with a neutral to negative zeta potential of ~-5 mV. The LNPs presented potent transfection capacity with the mRNA, but not with plasmid. Factorial analysis was used to identify optimal formulation conditions. Our early results indicate that the system has room for improvement, but presents potent transfection capacity, which merits further evaluation and presents potential for their subsequent analysis for oral delivery.

23. Computer-aided lead optimization of YM155 as an inhibitor of DNA topoisomerase IIα for the treatment of anaplastic thyroid cancer. **Colton**

Herrington, Luis Pena Marquez, Brian A. Salvatore, Elahe Mahdavian. LSU-Shreveport.

Abstract: Anaplastic thyroid cancer (ATC) is the most lethal form of all human cancers. One critical barrier to improving ATC's very poor prognosis is the lack of effective treatments. Thus far, surgery, radiation, and anti-cancer drugs have all failed to significantly prolong patient survival. Thus, there is an urgent need for new and effective drugs to treat this disease. Recent efforts, including a comprehensive NCI study, have led to significant interest in YM155 as a promising drug candidate for the treatment of ATC. This project is based on three important experimental observations. First, YM155 induces DNA damage and apoptosis by inhibiting DNA topoisomerase IIα (Top2a) in both cell culture and animal models of ATC. Second, Top2a expression and activity are directly correlated with the drug response. Thus, Top2a is a potential target of YM155, and its inhibition may contribute to YM155's mode of action as a cancer drug. Third, while YM155 displays potent anti-cancer activity both in vitro and in ATC mouse models, its performance in humans is relatively poor. In clinical trials for ATC, YM155 failed to demonstrate significant improvement over existing treatments. This poor clinical response is an obstacle we aim to address through the rational design of new bioisosteric analogs with higher binding affinity and better drug-like properties. In this project, we performed lead optimization through rational design of YM155 bioisosteric analogs followed by computational assessment of ADME properties and molecular docking for Top2a enzyme (PDB: 1ZXM). We identified a small set of YM155 analogs that are suitable for clinical development against ATC, exhibiting better binding affinity and superior ADME properties.

24. Inhibiting reelin inactivation: homology-based study of PCSKs and inhibition thereof towards arresting progression and cognitive loss in late-onset Alzheimer's. Conner Jaymes Howard, Seetharama D. Jois, and **Ronald A. Hill**. University of Louisiana – Monroe.

Abstract: Much evidence indicates that pathologies of late-onset (non-familial) Alzheimer's disease(s) (LOAD, >99% of cases) begin early within brain olfactory structures, thence propagating in an inflammaging-associated spatiotemporally consistent pattern. Genome-wide association studies (GWASs) of individuals who exhibit high LOAD pathology burden but remain cognitively normal suggest that select genetics can confer resistance to onset and progression. Reelin, a large glycoprotein component of the extracellular matrix (ECM), emerged from these GWASs as a central player in such preservation. Although best-known as a key player in embryo-fetal development, reelin in fact remains heavily involved during adulthood in dynamic brain maintenance and remodeling. Reelin's known adult-brain roles connect with other molecular-level processes having clearly established roles in LOAD, notably including those involving ApoE, and ones that govern microglial responsiveness states. In a handful of animal studies, intracerebral reelin could rescue cognitive function. Reelin (>3400 amino acids) incorporates multiple functionally relevant domains; fragments generated by cleavage at four specific sites exhibit trafficking and functions disparate from those of intact reelin. Loss of a 6-AA fragment from the C-terminus, through cleavage accordant with a proprotein convertase (PCSK) consensus sequence, inactivates reelin. As a first step towards exploiting this recent finding, a robustly studied liganded 3D structure of furin (PCSK3) served as the starting point for homology-based comparisons of additional candidate PCSKs for which no experimental structures are available, but for which complete or partial structures were generated by the AI-based Alphafold project (PCSK5, 6, 7). A docking protocol (Autodock) was validated with the furin:native ligand complex. Two inhibitors

were then designed for in-silico simulation with furin and PCSK5, the results of which will be shared in this poster.

25. Twinned Crystal Structure of N-(4-Methoxy-3-nitrophenyl)acetamide.

James Hines, Ogad A. Agu, Curtistine J. Deere, Frank R. Fronczek, Rao M. Uppu.
Southern University and A&M College and Louisiana Sate University.

Abstract: 4-Alkoxyacetanilides (4-AAs), in particular phenacetin, are mostly cleaved to give N-(4-hydroxphenyl)acetamide, the clinically relevant analgesic, while a small portion may undergo deacylation producing carcinogenic, kidney-damaging 4-alkoxyanilines. There has been extensive information on the phase I and phase II biotransformation of 4-AAs, but little is known about their biotransformation by non-enzymatic mechanisms including those mediated by nitric oxide-derived oxidants. Towards an understanding of this and shedding light on mol¬ecular targets, we have synthesized N-(4-methoxy-3-nitrophenyl)acetamide by acetylation of 4-methoxy-3-nitroaniline using acetic anhydride and purified by recrystallization from water. Single crystals of N-(4-methoxy-3-nitrophenyl)acetamide grown from water were analyzed by X-ray diffraction using Bruker Kappa APEX-11 Duo diffractometer. It was found that N-(4-Methoxy-3-nitrophenyl)acetamide crystallizes in monoclinic space group P21/n with Z=4 with a disordered nitro group in twinned crystals. Refinement using low temperature (90K) X-ray diffraction data yielded R=0.059 for 1675 reflections and 160 parameters. Both the methoxy group and the acetamide groups are nearly coplanar with the phenyl ring, with respective torsion angles of 0.0(4)° for C-C-O-Me and 4.9(4)° about the C-N bond to the ring. The C-N-C-O torsion angle is also insignificantly different from zero, 0.2(4)°. Overall, the 12-atom methoxyphenylacetamide group is coplanar to a mean deviation of 0.042 Å. The nitro group is twisted out of this plane by about 30°, disordered into two orientations with opposite sense of twist. The dihedral angle between the two disordered C-NO2 planes is 59.2°. The N-H group donates intermolecular hydrogen bonds with N...O distance 3.122(4) Å to nitro oxygen at x-1/2, 1/2-y, z-1/2, forming chains in the [1 0 1] direction. Interestingly, the amide carbonyl oxygen atom is not involved in hydrogen bonding. Combined with the recent revelations of mechanisms of action of N-(4-hydroxyphenyl)acetamide through indirect activation of CB1 receptors by 4-aminophenol and endocannabinoid reuptake inhibitor AM 404, the information presented here may provide useful insights into molecular targets for 4-AAs and their nitrated metabolites.

26. Metagenomic Analysis of Water and Soil in Grambling, Louisiana.

Thaddisha James, John Thomas, Lescia Valmond, Paul Kim, Audrey Kim.
Department of Biological Sciences, Grambling State University.

Abstract: Metagenomics, or the sequencing of genetic material collected from environmental sources, is used to research microorganisms found in soil and water. This metagenomic analysis of water and soil from the Grambling Pond and wastewater from Grambling State University (GSU) and the city of Grambling sewersheds will help us comprehend local biodiversity and uncover any antibiotic resistance genes present. We hypothesized that the profiles of microorganisms detected in these environments would be different based on our knowledge of microbial ecology. Conical tubes were used to collect water and sediment samples from the Grambling Pond and a 24-hour composite wastewater sample was collected from the wastewater lift stations at GSU and Grambling City. All water samples were centrifuged to obtain a pellet for DNA extraction using the ZymoBIOMICS DNA Miniprep Kit. DNA extraction from the soil samples was carried out using the DNeasy PowerLyzer PowerSoil Kit. DNA quality was assessed

by UV spectroscopy and DNA concentration was measured using a Qubit high sensitivity dsDNA assay. Libraries for sequencing were prepared using the Oxford Nanopore Rapid Barcoding Kit. Using the EPI2ME What's In My Pot bioinformatics pipeline, 867,885 reads were examined. Bacteria accounted for 94% of reads, 5% were classified as Eukaryota, and 1% were classified as Archaea / viruses. In overall taxonomic abundance, the top five species identified were Escherichia coli (111,351 reads), Homo sapiens (17,189), Cloacibacterium normanense (17,128), Sphaerotilus natans (6,700), Escherichia marmotae (4,851). Many of the identified species are enteric bacteria, which are naturally abundant in wastewater, but some were also detected in pond water and sediment. The EPI2ME Antimicrobial Resistance workflow produced 1,344 alignments to 185 genes in the Comprehensive Antibiotic Resistance Database. Future research will focus on how these microbes' antibiotic resistance affects water quality and public health.

27. Comparative Analysis of Strictosidine Synthase-Like Enzymes in Anticancer Alkaloid Biosynthesis. **Sara-Alexis Jarecki**, Audrey Lashley, Jessica Kading, Ryan Miller, and Vonny Salim. Louisiana State University Shreveport, Louisiana State University Health Sciences Center School of Medicine New Orleans.

Abstract: Monoterpene indole alkaloids (MIAs) are one of the most diverse classes of specialized metabolites that exhibit pharmaceutical properties. About three thousand MIAs have been characterized, the majority of which are produced by medicinal plants in the Apocynaceae family, such as Catharanthus roseus and Rauwolfia serpentina. A plethora of MIAs stem from a central intermediate compound, strictosidine, which is generated by strictosidine synthase. In Camptotheca acuminata, however, strictosidinic acid isomers serve as the precursor to produce the MIA camptothecin. Strictosidine synthase catalyzes the Pictet-Spengler-like reaction between iridoid secologanin and tryptamine in a stereospecific manner. Here, we characterize the key structural determinants within the active site that maintain the stereospecificity of Rauwolfia serpentina strictosidine synthase in comparison with candidates of potentially promiscuous strictosidinic acid synthases from Camptotheca acuminata. Furthermore, this study elucidates the evolutionary drivers in how medicinal plants adapt a unique six-bladed β-propeller protein fold to accommodate and combine two simpler precursors for diversification of plant natural products. The implications of this study will aid the development metabolic engineering platforms in altering the stereospecificity of plant alkaloids for drug discovery.

28. The Regiospecificity Control of Alkaloid Glucosidases in Medicinal Plant Camptotheca acuminata. **Jessica Kading**, Audrey Lashley, Ryan Miller, Stephanie Provenzano, and Vonny Salim. Louisiana State University Shreveport, Louisiana State University Health Sciences Center School of Medicine in New Orleans, Louisiana State University Health Sciences Center School of Medicine in Shreveport.

Abstract: Medicinal plant Camptotheca acuminata produces a DNA topoisomerase I inhibitor known as monoterpene indole alkaloid camptothecin. Although this compound has been widely used in the clinical settings, the manufacturing of camptothecin relies on tedious isolation from plant tissues with high cost. To increase the level of camptothecin production, metabolic engineering is proposed to provide solutions by reconstituting plant metabolic pathways into microbial systems. While the biosynthetic pathway to generate the central intermediate of alkaloids has been elucidated, the downstream camptothecin biosynthetic enzymes remain to be discovered.

The majority of monoterpene indole alkaloids are synthesized via the central intermediate strictosidine, however, Camptotheca acuminata does not accumulate this essential precursor. Instead, the camptothecin biosynthetic pathway in Camptotheca acuminata has been proposed to depend on the four stereoisomers of strictosidinic acids which are then deglucosylated by strictosidine glucosidase-like enzymes. Our reference strictosidine glucosidases from the monoterpene indole alkaloid-producing species, Catharanthus roseus and Rauwolfia serpentina, exhibit high specificity towards 3α-(S)-strictosidine, in comparison with the more promiscuous Camptotheca acuminata alkaloid glucosidases. In this study, we focused on the four candidates of alkaloid glucosidases from Camptotheca acuminata for structural modeling comparison to identify the key amino acid residues surrounding the hydrophobic pocket that control their regiospecificity. We anticipate this structural comparison will reveal the evolutionary insights of glucosidases in the plant kingdom to generate phytochemicals with enhanced biological activities.

29. Differential impact of PCP and its metabolite (TCHQ) on the immune mediators: in vitro study. **R. Kondati**, S. Thota, R. Begum, N. Bidarimath, D. Muthyala, W.C. Dorsey, and S. Batra. Southern University and A&M College.

Abstract: There is a consistent accumulation of immunotoxic substances in our environment causing cancer or damage to the immune system. Pentachlorophenol (PCP) is one such substance that was used as a pesticide and wood preservative in the United States. Literature survey also suggests that PCP was also used in the manufacturing of ropes, paints, adhesives, insulation, and brick walls. Therefore, the general population may be exposed to PCP through the use of textiles, leather, and paper products; and inhalation of indoor air contaminated with PCP. PCP is known to produce several toxic byproducts including tetrachlorohydroquinone (TCHQ), which has been linked to PCP's genotoxicity. While the studies from others and our laboratory provide significant evidence about PCP-induced inflammation/toxicity, there is a paucity of information about the role of TCHQ in regulating inflammatory responses. In light of these facts, we hypothesized that TCHQ exposure may result in a comparable immune regulatory effect to PCP in lung epithelial cells. Using human lung epithelial cells with type II characteristics (A549 cells) we, therefore, conducted comparative studies to elucidate the impact of PCP and TCHQ exposure on the key inflammatory mediators. Specifically, we challenged A549 cells with 10 μM and 25 μM PCP and TCHQ to determine the transcriptional regulation of cytokines/chemokines and transcription factors-NF-κB and STAT3. While the mRNA expression of CCL2 and IL-8 was higher in TCHQ-challenged cells, PCP exposure resulted in higher transcription of NF-κB and STAT3. We also observed a higher magnitude of TLR4-mRNA expression in PCP-challenged cells compared to the TCHQ-exposed group (25 μM; 24h). These observations suggest the possible differential impact of studied immunotoxic substances on the translational and post-translational regulations of immune modulators in A549 cells. We are conducting extensive studies to delineate the molecular mechanisms in detail.

30. GHRH antagonists protect against LPS-induced endothelial injury. **Khadeja-tul Kubra**, Nektarios Barabutis. School of Basic Pharmaceutical and Toxicological Sciences, College of Pharmacy, University of Louisiana Monroe.

Abstract: Introduction: Growth Hormone-Releasing Hormone (GHRH) is a neuropeptide which regulates the synthesis of growth hormone from the anterior pituitary gland. GHRH receptor (GHRH-R) is a G protein-coupled receptor, predominantly expressed in the pituitary gland. This hypothalamic hormone mediates the growth hormone-insulin like growth factor 1 (IGF-1) axis and

can promote malignancies. GHRH promotes inflammatory processes, while GHRH antagonists (GHRHAnt) can exert opposing activities. Lipopolysaccharides (LPS) can activate the Toll-like receptor (TLR) 4 to induce vascular leak, and that toxin is utilized in experimental models of lung injury. Herein, we investigate the effects of GHRHAnt in LPS-induced endothelial barrier dysfunction. Materials and Methods: The GHRH antagonist (#4030691) is available from Bachem. LPS (#L4130-500MG) was used to induce endothelial barrier dysfunction. Fluorescein isothiocyanate (FITC)-dextran assay was utilized to assess paracellular permeability in commercially available bovine pulmonary artery endothelial cells (BPAEC) (#PB30205) and human lung microvascular endothelial cells (HLMVEC-L) (#CC-2527). The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assessed cell viability. Results: GHRHAnt protects against LPS (1μg/ml) - induced barrier dysfunction via Cofilin and MLC2 modulation. In bovine cells, GHRHAnt post-treatment (1μM) counteracts the LPS-induced cofilin and MLC2 activation, while LPS (1μg/ml) and GHRHAnt (1μM) did not affect cell viability. In human and bovine endothelial cells, GHRHAnt post-treatment (1μM) suppresses LPS (1μg/ml)-induced paracellular hyper-permeability. Conclusions and future directions: GHRHAnt represent a promising therapeutic strategy against lung inflammatory disease. Future studies in inflamed mice will seek to support the in vitro data.

31. Protein-protein interaction between GleIF4E2 and GleIF2 is crucial in recruiting the ribosome onto the mRNA. **Francis Kwarteng**, and Srinivas Garlapati. University of Louisiana at Monroe.

Abstract: All eukaryotic cells and most lower eukaryotes, including yeast, fungi, and amoebas, contain a cap structure m7GpppN(m) consisting of 7-methylguanosine linked to the 5'end of the transcript by a 5'-5' triphosphate bridge. This posttranscriptional modification has been determined to play a crucial role in the cap-dependent initiation of protein synthesis by interacting with the eIF4F complex, which serves as a bridge in recruiting ribosome onto the mRNA. Giardia lamblia is a deep-branching eukaryote with different translation machinery than mammals. It has a very short mRNA 5' UTR. Homology studies of the parasite's genome have identified homologs for the eIF4F complex, which includes eIF4E and 4A but not for 4G, which is a scaffolding protein that recruits the ribosome onto the mRNA. Recent studies have revealed a novel protein-protein interaction between GleIF4E2 with GleIF2□. Studies involving Cryo-EM of yeast PICs have shown that eukaryotic initiation factor 2□ is close to the mRNA entry channel. Therefore, a possible mechanism for recruiting the mRNA to the entry channel of the ribosome might involve interactions between cap-bound Giardia initiation factor 4E2 with GleIF2□. GST-pull-down assays were performed to analyze the interactions between these two proteins to understand the mechanism of mRNA recruitment to the ribosome.

32. Structural Characterization for Diversification of Bioactive Compounds Generated by Anticancer Alkaloid Methyltransferase. **Audrey Lashley**, Ryan Miller, Stephanie Provenzano, Paul Erba, and Vonny Salim. Louisiana State University in Shreveport, Louisiana State University Health Sciences Center School of Medicine New Orleans, Louisiana State University Health Sciences Center School of Medicine Shreveport.

Abstract: Methylations, carried out by methyltransferases, are responsible for extensive cellular functions throughout life. In plants, numerous methyltransferases have been functionally characterized, especially those involved in the methylation of natural products. Medicinal plant

Camptotheca acuminata produces the monoterpene indole alkaloid (MIA) camptothecin, notable for its use as a chemotherapeutic agent. Due to the low abundance of this valuable compound in plants, metabolic engineering efforts have been pursued to increase its production in microbial system, while numerous biosynthetic enzymes in the late steps remain to be identified. In Camptotheca acuminata, 10-hydroxycamptothecin methyltransferase (Ca10OMT) has been biochemically characterized with broad substrate specificities because it accepted non-alkaloids (flavonoids and phenolics), unlike most alkaloid methyltransferases. The promiscuity of camptothecin biosynthetic enzymes in Camptotheca acuminata is further confirmed by the multiple isomers of alkaloids accumulated in plants. In this study, computational homology modeling of Ca10OMT revealed important amino acid residues that determines the substrate specificity, dimerization, catalytic mechanism, and the conservation of the Rossman-fold domain, a binding pocket for the methyl donor, S-adenosyl-L-methionine (SAM). The three-dimensional modeling with key amino acid residues of a unique methyltransferases, formation of the dimeric interface, hydrophobic pocket for substrate binding in Ca10OMT provides clarity for effective strategies in enzyme engineering, manipulating substrate specificity to accept chemical analogs, therefore increasing the chemodiversity of plant natural products with pharmaceutical values.

33. Examining gene expression profiles of Killifish brains with different life histories. **Chi Jing Leow** and Kyle Piller. Southeastern Louisiana University.

Abstract: The African Turquoise Killifish (Nothobranchius furzeri) is a model organism in the study of aging and age-related diseases. The Turquoise Killifish possess a life-span of 4-8 months making it a convenient experimental laboratory system. The accelerated life-cycle is associated with their natural occupancy of seasonal, ephemeral habitats in east Africa. Within the Nothobranchiidae, many species/genera are annual species, completing their life-cycle in less than a year, whereas others possess non-annual or facultative/semi-annual life-histories. The adult Turquoise Killifish brain exhibits the characteristics of aging such as neurodegeneration, learning impairment, and cognitive decline. In this study we examined the gene expression profiles of killifish brains with different life histories. RNA was isolated from adult killifish brains and sequenced using QuantSeq. Differential gene expression was conducted in pairwise comparisons between life-histories (annual vs. non-annual, annual vs. semi-annual, semi-annual vs. non-annual). More than 4,000 DEGs were observed between annual vs. non-annual species, 2,899 DEGs were observed between annual and semi-annual species, and 1,766 DEGs were observed between semi-annual and non-annual species. GO enrichment analysis showed down-regulation in biological processes including synapse organization, cell junction organization, synapse assembly, neuron development, and regulation of neuron project development in the annual species compared to the non-annual species. Overall the gene expression profiles of the killifish brains show similarity with our previous findings in liver tissue. Our GO enrichment analysis supports the idea that annual species have accelerated aging in the brains compared to the longer-lived species.

34. Synthesis and Identification of Functionalized Lactams as Potent Anti-Skin Cancer Agents: Modulators of Autophagy and Apoptotic Cascades. **MA Mahmud**, ST Boateng, RK Yadav, V Shearer, T Roy, JT Folahan1, B Donji, TK Beng and JC Chamcheu. University of Louisiana at Monroe and Central Washington University.

Abstract: Skin cancers (SC) are the most prevalent cancers in the U.S. affecting 9,500 people daily with an annual financial burden of $8.1 billion. The standard status quo for cutaneous melanoma (CMSC) and non-melanoma skin cancers (NMSCs) treatment are limited with low-bioavailability, side-effects, and drug-resistance. Recently, medicinal chemists are keen to escape flatland in view of exploring 3D space for the discovery of new drug entities. Thus, chiral nitrogen-containing cyclic compounds like piperazines/piperidines are valued targets for pharmaceutical companies. To increase drug availability, diversity-oriented synthesis (DOS) strategy aimed at producing drug-like compounds with a high degree of molecular diversity is a versatile tool in chemical biology and drug discovery programs. In this study, several functionalized lactams were synthesized and biologically screened against CMSC (SKMeL-28 /A375) and NMSC (A431/SCC-12) cell-lines in-vitro. Cytotoxicity evaluation identified potent hit-compounds with sub-micromolar anticancer activities with IC50 values: 0.85±0.1 μM(A375), 1.3 ±0.3 μM(SKMeL-28), 0.7±0.1 μM(A431) and 2.8±0.4 μM(SCC-12). Clonogenic and in-vitro wound closure/boyden chamber assays displayed dose-dependent decrease in clonogenicity and migration when treated with potent hits. Immuno-blotting/fluorescent analysis, apoptosis marker showed upregulation of Bax, cleaved caspase-3/9 and PARP levels while downregulating the expression levels of several cancer molecular targets including ERK1/2, PI3K/Akt and PIM3. Furthermore, the potent hits modulated autophagic pathway via modulation of Atg-5, Beclin-1, microtubule-associated protein 1A/1B-light chain 3 (LC3B), and SQSTM1/p62. Using SwissADME web-tool, PK profiling of potent hits displayed high skin-permeation (log KP), GIT absorption, Log Po/w (<5), compliancy to Lipinski rule and high biodegradable characteristics. Taken together, our data highlight promising novel lead-to-hit anti-skin cancer compounds.

35. Interactions of SA2 and S6E Ribosomal Proteins with EIF4E2 in Giardia lamblia. **Kade Malone**, Hailey Davis, Srinivas Garlapati, and Zach Wiggins. University of Louisiana Monroe.

Abstract: Giardia lamblia is a flagellated unicellular eukaryotic microbe that is responsible for diarrheal disease across the globe. The illness associated with infection of the organism, Giardiasis, affects over one million people annually. The key to treatment of this organism is better understanding of the organism's intracellular processes. Of these processes, the choice mechanism of study is translation initiation. Better understanding of translation initiation of Giardia lamblia will provide insightful information of how organism prepares to produce its proteins, and could be later used to inhibit this function, resulting in a better treatment of Giardiasis. The interaction studied was against Eukaryotic Initiation Factor 4E2 and surrounding proteins that may interact with it. Eukaryotic Initiation Factor 4E2 is part of the 4E family of proteins responsible for binding to the 7-methyl-guanosine cap of eukaryotic mRNAs. Proteins found in close proximity to EIF4E2 would be utilized for in vitro assays. The two selected proteins were SA2 and S6E which were found in very close proximity to EIF4E2. The purpose of these interaction assays that were ran was to identify new interactions in translation initiation and identify any changes to the translation initiation complex that may occur.

36. FHV-1 is unlikely to mutate in immunocompetent feline hosts treated with antiviral medication. **E.P. Mills**, A.C. Lewin, N.E. Ineck, M.A. Mironovich, M. Marino, C.C. Liu, U. Emelogu, P. Camacho, R.T. Carter. Department of Veterinary Clinical Sciences, School of Veterinary Medicine, Louisiana State University.

Abstract: Rationale: Feline herpes virus (FHV-1) is a common cause of ocular disease in cats. Multiple antiviral medications which target the UL23, UL30, and UL42 viral genome regions have been used as treatment for this disease. Compared to other herpes viruses such as herpes simplex virus (HSV1/2), FHV-1 has been shown to be highly conserved. Antiviral resistance has been previously documented in HSV 1/2 but has not been assessed with short term antiviral treatment in FHV-1 positive cats. Methods: Fourteen cats positive for FHV-1 from shelters in Louisiana, USA were assigned to one of four treatment groups: placebo (n=3), cidofovir 0.5% ophthalmic solution (n=3), famciclovir oral solution (90mg/kg; n=5), or ganciclovir 0.15% ophthalmic solution (n=3). Conjunctival swabs were collected on Day 1 and Day 8 after receiving twice daily treatment. DNA was extracted for sequencing using Illumina MiSeq with variant detection between each viral pair (Day 1/8). In-vitro half-maximal inhibitory concentration testing (IC50) for each non-synonymous viral pair was completed to assess for development of antiviral resistance. Results: 171 synonymous and 3 non-synonymous variants were identified between viral pairs. There were no variants in the UL23, UL30, or UL42 genes. A viral pair from each antiviral treatment group had one non-synonymous variant in the ICP4 region. The 3 non-synonymous variants did not show evidence of resistance when IC50 was evaluated. Conclusion: This data suggests that short-term use of various antiviral medications in FHV-1 positive immunocompetent cats is unlikely to mutate and result in antiviral resistance.

37. Subcellular Localization of Glucosidases for Anticancer Alkaloid Synthesis in Recombinant System. **Michael Minamyer**, Jessica Kading, Vonny Salim. Louisiana State University at Shreveport.

Abstract: Camptothecin is a topoisomerase inhibitor, a monoterpene indole alkaloid that is isolated from the Chinese happy tree (Camptotheca acuminata). Despite its application as a chemotherapeutic agent in the clinic, the purification of camptothecin relies on a tedious process of isolation from plant tissues. The removal of glucose moiety by alkaloid glucosidases is one of the critical steps in camptothecin biosynthesis. While the majority of monoterpene indole alkaloid-producing plant species utilize specific stereoisomer of strictosidine before the deglycosylation step to produce diverse alkaloids, camptothecin synthesis in Camptotheca acuminata involves multiple isomers of strictosidinic acids with potentially promiscuous biosynthetic enzymes. In this study, the behavior of one strictosidinic acid glucosidase (CaAGD1) from Camptotheca acuminata is further explored by determining their subcellular localization for the prospect of metabolic engineering in a recombinant system. The most promiscuous Camptotheca acuminata alkaloid glucosidases, CaAGD1 is fused with yellow fluorescence protein (YFP) for expression in Nicotiana benthamiana and visualization via fluorescence microscopy. We showed that CaAGD1 is localized in the nucleus, similar to previously characterized Catharanthus roseus strictosidine glucosidase. The localization of biosynthetic enzymes will further inform the metabolic engineering efforts in targeting multiple biosynthetic enzymes within a minimum number of compartments for efficient metabolic flux in host microbial or plant systems. This effort will also assist further elucidation of camptothecin biosynthetic pathways and cellular machineries in producing alkaloids with high pharmaceutical values.

38. Computational methods for development of arbidol as a fusion inhibitor of the novel coronavirus. **Alireza Moosavi**, Elahe Mahdavian, Scott Chirhart. LSUS, Centenary College of Louisiana.

Abstract: The novel SARS-CoV2 is a highly pathogenic virus and the causative agent of COVID-19 disease. There are currently very limited number of FDA-approved drugs for COVID-19, and thus an unmet medical need for new and effective therapeutics against this deadly virus. In this project we use a computer aided drug discovery (CADD) approach to rapidly identify promising drug candidates against COVID-19. Using prior knowledge of existing anti-viral drugs, we chose arbidol, an anti-influenza drug, as a seed compound for this project. Arbidol has shown significant anti-viral activity against SARS-CoV2 in various pre-clinical disease models of the virus. However, despite its promise, as a drug, arbidol displays several limitations, including large conformational flexibility and poor water solubility. Using medicinal chemistry insights and Swiss-Bioisostere tool, we assembled a medium-size drug library of compounds with structural modifications to address arbidol's known drug limitations. We also chose the SARS-CoV2 fusion protein (Spike: S2) and a high-quality structural model, PDB-ID: 6VXX, as the protein target for this computational drug discovery project. We hypothesized that arbidol and certain analogs can act as fusion inhibitors against SARS-CoV2 since the viral spike protein binds to the host receptor protein (ACE2) through a similar mechanism as Influenza's hemagglutinin. We employed molecular docking to assess the binding affinity of the drug candidates to Spike protein (6VXX) and screened the ADME parameters using Swiss-ADME tool for each compound, removing analogs with low binding affinity and undesirable physiochemical characteristics. Analysis of binding energies/interactions in compound-6VXX complexes and ADME properties was used to prioritize compounds for the validation of their anti-viral activity in experimental research. The goal to is select the most promising compounds that can serve as fusion inhibitors of the SARS-CoV2 viral infectivity mechanism.

39. The Tobacco β-Cembrenediol: A Promising Prostate Cancer Recurrence Suppressor Lead via Modulation of Indoleamine 2,3-Dioxygenase and Tryptophan Dioxygenase. **Ethar Mudhish**, Abu Bakar Siddique, Hassan Y. Ebrahim , Khaldoun S. Abdelwahed , Judy Ann King and Khalid A. El Sayed. University of Louisiana Monroe, LSU Health Shreveport.

Abstract: Prostate cancer (PC) is the second leading cause of death in men in the US. PC has a high recurrence rate, and limited therapeutic options are available to prevent disease recurrence. The tryptophan-degrading enzymes 2,3-indoleamine dioxygenase (IDO1) and tryptophan dioxygenase (TDO2) are upregulated in invasive PC. (1S,2E,4R,6R,7E,11E)-2,7,11-cembratriene-4,6-diol (β-CBT) and its C-4 epimer α-CBT are the precursors to key flavoingredients in tobacco leaves. Nearly 40-60% of α- and β-CBT are purposely degraded during commercial tobacco fermentation. Earlier, β-CBT inhibited invasion, reversed calcitonin-stimulated transepithelial resistance decrease, and induced tighter intercellular barriers in PC-3M cells. This study demonstrates the in vitro β -CBT antimigratory (wound-healing assay) and anti-clonogenicity (colony-formation assay) activities against five diverse human PC cell lines, including the androgen-independent PC-3, PC-3M, and DU-145, the castration-recurrent CWR-R1ca, and the androgen-dependent CWR-22rv1. Meanwhile, β -CBT potently suppressed in vivo locoregional and distant recurrences after the primary tumor surgical excision of PC-3M-Luc cell tumor engrafted in male nude mice. β -CBT treatments suppressed organ and bone metastasis and lacked any major toxicity over the 60-day study course. β -CBT treatments significantly suppressed IDO1, TDO2, and their final metabolite kynurenine levels in PC-3M cells. β -CBT treatments significantly suppressed the tumor recurrence marker PSA and kynurenine levels in treated animals' plasma. β -CBT emerges as a promising PC recurrence suppressive lead.

40. Possible role of 19S proteasome in e-cigs induced inflammation. **D. Mutyala**, R. Begum, S. Thota, N. Bidarimath and S. Batra. SOUTHERN UNIVERSITY A&M COLLEGE.

Abstract: The use of e-cigarettes has rapidly gained popularity due to their extensive marketing as a safer alternative to conventional smoking. However, recent investigations suggest that the molecular consequences of vaping are quite similar to conventional smoking. Earlier studies demonstrate that exposure to e-cig vapor condensate (ECVC) alters biological pathways involving protein homeostasis. The findings from our laboratory demonstrate the important role of inducible catalytic subunits of 20S proteasome (immunoproteasome) in ECVC-induced inflammation/cellular homeostasis. However, the preparatory steps involving the substrate binding and commitment; and gate (19S) opening of the 20S proteasome are equally important in ubiquitin-mediated degradation of proteins. In this regard, the regulation and role of regulatory subunits and deubiquitylating enzymes which are the components of 19S gate/cap have not been well studied in ECVC-exposed cells. While Rpn10 is associated with the degradation of proteins with single chains of K48-linked ubiquitin, Rpn13 has been shown to retard the degradation of various single-chain substrates in earlier studies. Interestingly, proteins with multiple short ubiquitin chains can be targeted more efficiently for degradation by proteasomes through the ubiquitin-like domain, when bound by Rpn13. On the contrary, deubiquitylating enzymes-UCHL-5 cleaves 'Lys-48'-linked polyubiquitin chains, while Rpn11 possesses isopeptidase activity in the proteasome. Our results demonstrate an increase in the transcription and translation of 19s subunits- Rpn10, Rpn-11, Rpn-13, and UCHL-5 in TF-ECVC-challenged cells. While we also observed an increase in NF-κB activation and IκBα degradation in ECVC-challenged cells, the latter being a substrate for the Rpn13/UCH37 complex. Overall, our findings provide evidence about the possible role of 19S gate subunits in the ECVC-induced inflammation.

41. Crystal Structure of Racemic Bucetin, N-(4-Ethoxyphenyl)-3-hydroxybutanamide: Significance to Mechanisms of Toxicity of Phenacetin. **Zechariah Myles**, James E. Hines III, Garrick Breaux, Frank R. Fronczek, Rao M. Uppu. Southern University and A&M College.

Abstract: Bucetin is an analgesic and antipyretic that is similar in structure to phenacetin. Once thought to be a better substitute for phenacetin, bucetin was introduced into the markets in Germany but was soon withdrawn from use due to renal toxicity. The renal toxicity of bucetin, renal papillary necrosis, is like that induced by phenacetin but is somewhat less pronounced, presumably due to a difference in the rate of deacylation by microsomal enzymes leading to the formation of 4-ethoxyaniline. Thus, the renal papillary necrosis by phenacetin and bucetin appears to be a manifestation of the formation of 4-ethoxyaniline and the subsequent inhibitory action of this putative metabolite (or its hydroxylated and/or autooxidation products, N-(4-ethoxyphenyl)hydroxylamine and 1-ethoxy-4-nitrosobenzene) on PGE2 synthesis and the possible reduction of COX-2 expression. However, unlike the case with phenacetin, there is limited or no information on chlorinated, nitrated, or other metabolites of bucetin likely to be formed in vivo through cellular oxidants. To address this and to better understand the mechanisms of toxicity of bucetin, we determined the crystal structure of racemic bucetin analyzed using a Bruker Kappa APEX-II DUO diffractometer. Single crystals of bucetin were prepared by slow cooling of a nearly saturated solution of bucetin in boiling water (resistance: 18.2 MΩ/cm). The racemic bucetin crystallizes in monoclinic space group P21/c with Z=4. Refinement using low temperature (100

K) X-ray diffraction data yielded R=0.045 for 2139 reflections and 153 parameters. The molecule is in an extended conformation, with 170.14(15)° C-O-C-C torsion angle in the ethoxy group and torsion angles C-N-C-C -177.24(16)°; N-C-C-C 170.08(15)°; C-C-C-C 171.41(15)° in the butanamide chain. The OH group donates an intermolecular hydrogen bond to amide carbonyl oxygen and accepts an intermolecular hydrogen bond from N-H. The geometries of these hydrogen bonds are 2.7268(17) Å for OH...O (at 1-x, 1-y, 2-z) and 2.8611(19) Å for NH...O (at x, 1/2-y, z-1/2). The former thus forms 12-membered dimeric rings about inversion centers, and the latter form chains in the [0 0 1] direction. The overall hydrogen-bonded network is two-dimensional, with no propagation in the [1 0 0] direction. Given the current understanding that de-acylation constitutes an important step in the expression of renal toxicity, and the fact that the acyl group in bucetin (3-hydroxybutyrate) is much larger compared to the acetyl group in 4-alkoxyacetanilides and has a chiral center, the information on bucetin crystal structure presented here may help in the development analgesics with little or no renal toxicity.

42. Computational Investigations of Stereospecificity In Concerted Electrocyclic Reactions. **William A. Parkinson**, and Grant Meadows. Southeastern Louisiana University.

Abstract: Successful drug design relies on the synthetic chemist's ability to optimize Structure-Activity Relationships (SARs) of specific functionalizing moieties. Instead of exploring pharmaceutical design via traditional laboratory combinatorial methods, this project proposes to use computational quantum chemical techniques to explore the energetics of reaction pathways of concerted synthetic processes tailored to systems important in drug design. Specific applications include the theoretical investigation of thermodynamic and kinetic control in heterocyclic ring formation intended as drug delivery vehicles. Computational methods will also be used to predict stereospecificity of drug functionalization that results from Diels-Alder and retro-Diels-Alder processes.

43. The Basic Emergency Guidance Instrument: A Training Device for Bag Mask Ventilation. **Ankit Patel**, Phillip C.S.R. Kilgore, J. Steven Alexander, Marjan Trutschl, Luke White , Urška Cvek. Louisiana State University Shreveport, LSU Health Sciences Shreveport.

Abstract: Over-bagging or too frequent delivery of breath is commonly a result of failing to perform manual respiration using an AMBU bag. Bag Mask Ventilation (BVM) is a notoriously difficult skill to master, and although it is most often required in emergency situations, improper utilization of BVM can exacerbate a patient's condition or even lead to patient death. The Basic Emergency Narrated Guidance Instrument (BENGI) is an airflow monitor aimed at training medical personal to avoid these injuries. We took measurements from participants who provided a per training sample, trained with the device, and then waited a two-week period for the post training. Delivering between 300 and 600 mL or 8 to 15/min was considered adequate ventilation for the purpose of assessing performance. We compared the users that trained with the BENGI for a 4-day period to users that did not. We observed a statistically significant improvement in the Tidal Volume and Respiratory Rate.

44. Topiramate modulates nicotine withdrawal in mice. **Erika Perez**, Shannon May. Xavier University of Louisiana.

Abstract: Tobacco use is highly prevalent in alcohol dependent individuals. Topiramate is an FDA approved anticonvulsant medication that has been used off-label for the treatment of alcohol use disorders. Topiramate reduces alcohol consumption and has been also shown to reduce smoking behavior in heavy drinkers. The ability of topiramate to reduce smoking in non-alcohol dependent users is still under investigation. The goal of this study was to understand how topiramate modifies nicotine withdrawal associated behaviors in nicotine only dependent mice. Animals were treated with nicotine for a minimum of 6 weeks via the drinking water, vehicle control groups were also used. On test day control-treated, nicotine-satiated and nicotine-withdrawal mice were treated with topiramate and physical signs were recorded. Similar to our previous studies in alcohol, topiramate was able to precipitate physical symptoms in nicotine satiated mice. Unlike our previous results, topiramate did not reduce withdrawal symptoms. Anxiety-like behavior was also measured in the elevated plus maze and tail suspension test. Our results suggest that topiramate treatment does can alter nicotine withdrawal, however it is distinct than what has been observed with ethanol. GluK1-containing kainate receptors (GluK1*KARs) are non-selectively inhibited by topiramate and genetic association studies suggest that this receptor system moderates the reduced drinking in AUD patients. Our results support the continued study using more selective antagonist to understand the connections between GluK1*KARS and nicotine withdrawal.

45. Targeting HER2 dimerization for non-small cell lung cancer (NSCLC) by peptidomimetic: Effect of HER2 knockdown on dimerization of EGFRs and specificity of peptidomimetic. **Vivitri Prasasty**, Prajesh Shrestha, Debajyoti Majumdar, Arpan Chowdhury, Daniel Billadeau, Yong-Yu Liu, Seetharama D. Jois. School of Basic Pharmaceutical and Toxicological Sciences, College of Pharmacy, University of Louisiana Monroe, Division of Oncology Research, Mayo Clinic.

Abstract: Epidermal growth factor receptor (EGFR) is a major oncogenic driver of NSCLC. Among the EGFR family of receptors, HER2 overexpression, amplification, and mutation play an important role in developing resistance to targeted antibodies and tyrosine kinase inhibitors (TKIs). We have designed and evaluated novel peptidomimetics to inhibit the dimerization of EGFRs in HER2-positive (HER2+) breast cancer and NSCLC cells. Our objective is to evaluate the effect of the compound SFTI-G5 in 3D cell culture models and to evaluate the specificity of the peptidomimetic to target HER2 protein in NSCLC. We used different 3D cell culture procedures, including the hanging drop method and Ultra-low attachment plate method, to form spheroids and analyzed antiproliferative and anti-tumor efficacy. Anti-tumor activity of the compounds was determined by observing the spheroid volume calculated from the images of the spheroids taken from day 1 to day 5. SFTI-G5 was shown to reduce the 3D spheroid volume in HER2-positive 3D spheroids. To evaluate the specificity of SFTI-G5 to HER2 overexpressed NSCLC cell lines and to see the effect of each EGFR protein for dimerization, we wanted to knockdown EGFR, HER2, and HER3 proteins in Calu-3 lung cancer cell lines. Six lentiviral shRNA knockdown plasmids containing EGFR or HER2, or HER3 knockdown were prepared. The knockdown cells were evaluated for EGFR and HER2 expression using fluorescently labeled antibodies. Further, to evaluate the specificity of SFTI-G5 for HER2, a PDX mouse model of HER2 knockdown was used. In vivo studies on the PDX model indicated that SFTI-G5 was not able to suppress tumor growth in the HER2 knockdown PDX model. Our studies indicated that SFTI-G5 specifically targets HER2 protein and inhibits the dimerization of HER2 with other receptors. Thus, SFTI-G5 will be useful for developing therapeutic agent for HER2 positive lung and breast cancer. Funding

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46. Characterization of Hsc70 interactions regulating LPS stimulated RAW264.7 cells. **John Rakus.** University of Louisiana at Monroe.

Abstract: The central hypothesis for this LBRN Start-Up proposal is that comprehensively defining Hsc70 interactions with client and non-client proteins will clarify intricacies in the regulation of lipopolysaccharide (LPS) regulation with toll-like receptor 4 (TLR4) to activate tumor necrosis factor α (TNFα). This signaling pathway is crucial to evoking a robust inflammatory response to bacterial infection but uncontrolled production of TNFα can be extremely hazardous to the host. Substantial evidence supports a contribution by Hsc70 in augmenting LPS-induced TNFα secretion. A fuller understanding of the role of Hsc70 in modulating this critical innate immune response is therefore crucial to being able to completely understand the overwhelming production of TNFα in diseases such as rheumatoid arthritis and sepsis can be addressed. The central hypothesis of this proposal will be evaluated via the following specific aims: Specific Aim 1: Validation of murine Hsc70 clients through co-immunoprecipitation and western blotting. Specific Aim 2: Validation of Hsc70 client interactions identified in human cells that also occur during LPS response in murine macrophages. Specific Aim 3: Delineation of Hsc70 binding interactions relevant to LPS response in murine macrophages though TNFα activation assays. In order to execute these aims, mouse RAW264.7 macrophage-like cells will be exposed to varying concentrations of LPS and subjected to immunoprecipitation assays to extract and identify proteins binding to Hsc70. Using a combination of previously conducted mass spectrometry assays with co-immunoprecipitation, western blotting, TNFα activity assays, and transfections, novel Hsc70 interactions will be identified and the effects of these on precise molecular events within the LPS/TLR4 regulatory pathway will be elucidated. Completion of the project will enhance understanding TNFα activation and regulation and characterize Hsc70 function in a crucial immune process.

47. Development of therapeutic drugs for Alzheimer's Disease. **Dylan Roberts**, Santosh D'Mello, Hailey Brokenberry, Autumn Sanderson. Louisiana State University Shreveport.

Abstract: Excitotoxicity is a form of neuronal cell death caused by atypically high levels of the excitatory neurotransmitter, glutamate, resulting in the overstimulation of the NMDA receptor, a subtype of ionotropic glutamate receptors. Several studies have found that excitotoxicity contributes to the pathological loss of neurons in Alzheimer's disease and other neurodegenerative diseases. Clinical trials have yet to provide an effective therapy for Alzheimer's disease, a disease characterized by progressive decline in memory and other cognitive functions. A long-term objective of our lab is to understand the cellular and molecular mechanisms underlying Alzheimer's as a step towards identifying drugs that can protect neurons against neurodegeneration. Because a major site of neuronal loss in Alzheimer's disease is the hippocampus, we have chosen HT22 cells, mouse hippocampally-derived cell line, to establish a cell culture model of excitotoxic death for the testing of candidate neuroprotective compounds. We conducted a dose-response analyses using glutamate and determined that it kills HT22 cells in a dose-dependent manner with substantial death starting at 2.5 mM. Unexpectedly, given the excitotoxic action of glutamate is mediated by activation of the NMDA receptor, treatment of differentiated and undifferentiated HT22 cells with NMDA had no effect on cell viability even at relatively high concentrations. These results suggest that the toxic effect of glutamate in

undifferentiated HT22 cells is due to a mechanism other than excitotoxicity, and likely to be excessive oxidative stress. We have demonstrated protection by testing candidate neuroprotective compounds including GW5074, a commercially-available inhibitor of c-Raf, a Src family kinase inhibitor SU6656 (SU), and an inactive form of PKR inhibitor (PKR). While GW5074 was partially protective, SU and PKR were completely protective against glutamate toxicity at doses at or greater than 250 mM and 500, respectively.

48. Development of Multifaceted Strategies in Elucidation of Anticancer Plant Natural Product Biosynthetic Pathways. **Vonny Salim**, Jack Baricuatro, Audrey Lashley, Sara-Alexis Jarecki, Jessica Kading, Michael Minamyer, Ryan Miller, Paul Erba, Stephanie Provenzano, Keelin North, Elahe Mahdavian, Urska Cvek, and Shile Huang. Louisiana State University Shreveport, Louisiana State University Health New Orleans, Louisiana State University Health Shreveport.

Abstract: Plant natural products are excellent sources of anticancer therapeutics. For enhanced productions, the functional characterizations of their biosynthetic enzymes are necessary prior to metabolic engineering for more efficient expressions in microbial systems. The integrative approaches are developed to identify these biosynthetic genes by mining the medicinal plant genomes, transcriptomes, and metabolomes. In this case, we applied these strategies with Camptotheca acuminata, producing alkaloid camptothecin. Unlike any other alkaloid producing species, C. acuminata utilizes multiple isomers of intermediates and homologous enzymes to form camptothecin in organ-specific manners. Further enzyme assays show that several camptothecin biosynthetic enzymes have broader substrate specificities in accepting multiple isomers of alkaloid substrates, and even non-alkaloids, such as flavonoids. By combining this knowledge with structural biochemistry, we anticipate further advancements in altering the substrate specificities of plant natural product biosynthetic enzymes for generating new-to nature compounds. This rational-design approach is also complemented by the examination of "deconstructed" molecular backbone of electroactive natural product (electrochemical synthon), using flavonoid quercetin as an example. This effort will extract structure-reactivity relationships engendered by the strategic modification of the molecular template with foreign substituents that typify special steric and electron-withdrawing/donating properties. The conceptual framework using electrochemical experiments that focus on the characterization of the potential-dependent adsorption behavior of each synthon underpin the atomic-level understanding of antioxidant properties of selected bioactive natural products. Ultimately, this technique will support the development of robust structure-based drug design of plant-derived compounds for improved pharmaceutical properties.

49. Microwave-assisted synthesis of phenyl methylene bis- pyrazolones. **Rabina Sapkota**, Atchimnaidu Siriki, Denzel EI Hage, Siva Murru. University of Louisiana Monroe.

Abstract: Most natural compounds and synthetic drug molecules have heterocyclic moieties which are responsible for biological functions. Our research group focus on the design, synthesis and biological evaluation of nitrogen heterocyclic compounds. We have investigated the effect of these pyrazolone derivatives as potential anticancer agents against skin and lung cancer cells. Although we achieved good potency, we still need to improve the selectivity index against cancer cells over the non-cancerous cells. In continuation of our efforts in achieving high selectivity and potency, we are currently developing new pyrazolone molecular hybrids using variety of synthetic

approaches. Along those lines, we have developed microwave reaction conditions for the synthesis of a series of phenylmethylene bis-pyrazolones. Synthesis involves the condensation of pyrazolone derivatives with an aldehyde and a secondary amine to produce phenylmethylene bis-pyrazolone derivatives. We have fabricated various benzylidene molecular hybrids by optimizing the reaction parameters, such as solvents, microwave power, reaction time, and temperature. We have confirmed the structure of the final product using single crystal X-ray crystallography. All the synthesized compounds were evaluated for in vitro anticancer activity against human melanoma (A375 and SK-Mel-28) and non-melanoma (A431 and SCC-12) cancer cells. Reaction development, synthesis and structural characterization of the final products will be discussed in the poster.

50. Stable upregulation of miR-143 and miR-506 decreases cell proliferation and cell cycle progression in lung cancer cells. **Archana Shrestha**, Behnaz Lahooti, Constantinos M. Mikelis, George Mattheolabakis. School of Basic Pharmaceutical and Toxicological Sciences, College of Pharmacy, University of Louisiana at Monroe, Department of Pharmaceutical Sciences, Texas Tech University Health Sciences Center, Department of Pharmacy, University of Patras.

Abstract: Among the cancer-related deaths in the United States, lung cancer is the most frequently observed, with a dismal five-year survival rate of ~22%. Small RNA therapeutics have played a significant role for cancer treatment, with micro-RNAs (miRs) being on the forefront in these efforts. miRs, small noncoding RNAs, are part of the cell's RNAi mechanism capable of gene expression regulation. In our prior study, we reported on miR-143 and miR-506's transient transfection's capacity to induce apoptosis and cell cycle inhibition, associated with cyclin dependent kinase (CDK) downregulation. In this study, we developed lentiviral-mediated stable deregulations of the miRs in A549 cells, individually or in combination. Using fluorescence activated cell sorting (FACS), we collected the highest GFP-fluorescence expressing cells and confirmed the miR deregulation using quantitative real-time polymerase chain reaction (qRT - PCR), as well as performed cell cycle analysis using Flow cytometry. TaqMan qPCR showed over five times of the basal expression for the respective miRs in the stable upregulation groups, and a respective approximately >50% downregulation of the two genes for the stable downregulation groups. The cell cycle analysis indicated a complex behavior for the individual miRs, whereas the combination upregulation of the two miRs indicated a G2 inhibition. Our results support that the miR combination upregulation induces a G2 arrest in opposition to the respective downregulations, while the deregulation of the individual miRs were demonstrating a complex, undefined behavior. This was supported by an increase in cell doubling time for the combinatorial miR upregulation. This work reinforces the potential of the two miRs for lung cancer treatment, which merits further evaluation.

51. Alanine scanning and pharmacokinetics of a grafted peptidomimetics that targets EGFR dimerization: Implications in NSCLC. **Prajesh Shrestha**, Arpan Chowdhury, Seetharama D. Jois. School of Basic Pharmaceutical and Toxicological Sciences, College of Pharmacy, University of Louisiana Monroe.

Abstract: Dimerization of epidermal growth factor receptors (HER1, HER2, HER3, and HER4) due to overexpression/mutation or ligand binding is responsible for generating enhanced signaling

leading to cell growth and tumor progression. Inhibiting EGFR:HER2 and HER2:HER3 dimerization have significantly impacted HER2 overexpressed lung cancer, in particular, non-small cell lung cancer (NSCLC). Targeting EGFR dimerization has been done using a variety of novel approaches, including peptide therapies. However, Peptides and peptidomimetics come with the inherent disadvantage of low stability. Hence, we have used Sunflower trypsin inhibitors as a stable framework to graft the peptidomimetic (compound-18) to develop a new compound, SFTI-G5. The effectiveness of SFTI-G5 has been demonstrated in several in-vitro and in-vivo models, and it has previously demonstrated excellent resistance against thermal and enzymatic degradation. With an IC50 value of 73 nM in the Calu-3 cell line and 369 nM in the A549 cell line, it inhibited tumor progression in various HER2-positive cancer cell lines. Previous studies have shown the compound to have anti-tumor activity in xenograft models; hence this study aims to evaluate the pharmacokinetic profile of SFTI-G5 when administered intravenously and orally. Similarly, to understand the importance of the side chain on peptide bioactivity, we used alanine scanning, which has been widely employed to identify binding residues in short peptides. Various analogs were synthesized by replacing each amino acid with alanine, and the antiproliferative activity of these compounds was seen in various cell lines. Pharmacokinetic studies on SFTI-G5 via tail vein injection in mice showed a rapid distribution and indicated a terminal half-life of 42 h. When it was administered orally, it showed that the PK of the compound follows a two-compartment model with peptide concentration reaching maxima at 30 min and 8 h in serum. Preliminary alanine scanning showed a relative decrease in the antiproliferative activity of various analogs compared to the parent compound, thus suggesting the importance of various peptide side chains on the activity of the parent compound (SFTI-G5). Funding for this project was supported by the National Cancer Institute (NCI) of the National Institutes of Health (NIH) 5R01CA255176-02 to SJ and DB.

52. Role of DAMPs in regulating Inflammation and autophagy process in pentachlorophenol challenged lung and liver epithelial cells. **Shilpa Thota**, Rizwana Begum, Nandini Bidarimath, WC. Dorsey, Sanjay Batra. Southern University A & M college, Grambling State University.

Abstract: Pentachlorophenol (PCP) was a widely used organochlorine pesticide and wood preservative in the U.S. Due to its carcinogenic activity, the use of PCP was restricted by EPA. PCP is easily absorbed through the skin and lungs. Since it is an environmental toxicant, chronic exposure leads to severe lung and liver toxicity in humans. There are few reports which demonstrate PCP-mediated increase in inflammatory responses and autophagy in various study models. The autophagy process plays a critical role in regulating the expression of inflammatory mediators, protein homeostasis, and cell survival. However, the associated molecular mechanisms are yet to be explored in detail. We used human lung adenocarcinoma cells (A549) and human liver carcinoma cells (HepG2) challenged with 1 and 10μM PCP for 24h as our study model. Our findings demonstrate increased production of cytokines/chemokines; production and release of danger-associated molecular patterns (DAMPs) including heat shock protein 70 (Hsp70) and High mobility group box protein 1 (HMGB1); and expression of several autophagy proteins (Beclin-1, LC3B, ATG12, ATG16) by PCP-challenged A549 and HepG2 cells. We thus hypothesized that DAMPs play a critical role in regulating the autophagy process in PCP-challenged lung and liver cells. In this regard, we observed molecular interactions between Hsp70, TLR4, and Beclin1 in PCP-challenged A549 cells. Furthermore, antibody-mediated neutralization and knockdown of Hsp70 showed abrogated-1) cytokine/chemokine (IL-6, IL-8) production; 2) expression of

transcription factors (NF-kB, STAT3) and autophagy-related proteins (Beclin1 and LC3B) in PCP-challenged cells. Our results will provide important information about molecular events responsible for regulating the autophagy process during PCP exposure in our study model(s).

53. Effects of Arginine on Antimicrobial Activity of AMPs. **Samantha Townsend**, Kathleen Pierce, Dale Major, Rebecca Giorno, Scott Poh. Louisiana Tech University.

Abstract: The recent increase of multidrug resistant bacteria poses a serious threat to public health. A promising alternative to combat antibiotic resistance is antimicrobial peptides (AMPs). AMPs are relatively short peptide chains that typically range from 10 to 70 amino acid residues and show antimicrobial activity. Although AMPs tend to have less toxicity than antibiotic therapeutics, they have proven to have a broader range of activity and a lower potential for resistance development. The most promising AMPs are those with shorter sequences because they are more easily able to penetrate the cell membrane of target cells. In this study, two previously identified AMPs RR and RIKA were modified by the addition of two arginine residues to the N-terminus 2(Arg)-RR and 2(Arg)-RIKA. These modified peptides were synthesized using solid phase peptide synthesis and evaluated for antimicrobial activity against E.coli and S.epidermidis with a minimal inhibitory concentration (MIC) assay. RR and RIKA have previously demonstrated consistent antimicrobial activity against E.coli and S.epidermidis. In this study, 2(Arg)-RR and 2(Arg)-RIKA demonstrated antimicrobial activity, however at higher MICs than RR and RIKA.

54. Development of green methods for the synthesis of drug scaffolds. **Mark Trudell**, Brooke N. Diehl, Danielle E. Allen, Annika Beaverson. Department of Chemistry, University of New Orleans.

Abstract: The kaolinite-related clay, halloysite (Hal), has been identified as a solid support for numerous chemical applications. The morphology of Hal particles is highly diverse, but the most common shapes are elongated, curled particles that form nanotubes or nanoscrolls. Hal nanoscrolls are generally 0.2-2 μm in length, having an inner diameter size of 10-40 nm and an outer diameter size of 40-70 nm. We have recently shown that transition metal nanoparticles(MNP) encapsulated in halloysite afford highly reactive catalytic systems for organic transformations in aqueous media. We have prepared and characterized a variety of nanocomposites of MNP encapsulated in halloysite (M@Hal). Preliminary studies have shown Cu@Hal and Pd@Hal to possess remarkable catalytic activity under green chemistry conditions for the preparation of a variety of important drug scaffolds. The scope and limitations of Cu@Hal and Pd@Hal for the green synthesis for several common drug scaffolds will be presented.

55. Expression of GAD isoforms in the adult mouse olfactory epithelium. **Jeremiah Vance,** Kylie White, Kathryn A. Hamilton, Stephanie L. Villalba. LSU-Shreveport, LSU Health-Shreveport.

Abstract: During the development of cortical neurons, the neurotransmitter GABA influences the migration of the neurons and their formation of functional synapses, activity of which deters apoptosis. In the olfactory system, synaptic activity also appears to be required for survival of olfactory sensory neurons (OSNs), which are located in the olfactory epithelium. The OSNs, unlike cortical neurons, can be generated throughout life, by progenitor cells lying deep within the OE. It therefore seems reasonable that, due to its lifelong regenerative capacity, the adult OE might express glutamic acid decarboxylase (GAD), the synthetic enzyme responsible for synthesizing

GABA from L-glutamic acid. For this project, we propose to use transgenic GAD65-GFP mice, in which the promoter for the 65 kDa isoform of the glutamic acid decarboxylase (GAD) gene drives expression of eGFP. These mice have been used to study GFP+ inhibitory interneurons located throughout the central nervous system, but the adult MOE has not been carefully studied. Our preliminary results show that the OE of GAD65-GFP mice contains GFP+ OSNs that are immature. The results further show that the OE expresses mRNA for both isoforms of GAD, GAD65 and GAD67. Expression of GAD65, GAD67, and GABA by the GFP+ OSNs and/or their progenitor cells would suggest that GABA plays a role, e.g., in turnover of the OSNs, axonal outgrowth, and/or formation of new synapses in the olfactory bulb.

56. Modified bacteriophage integrase lambda integrase can recombine attP-like sequences from human genome. **Yuri Voziyanov**, Joe D. Williams. LA Tech University.

Abstract: Bacteriophage lambda integrase (Int), which belongs to the tyrosine family of site-specific recombinases, can perform a full spectrum of genome rearrangements: integration, deletion, inversion, and replacement of DNA fragments which can make it an excellent genome editing tool. The genome editing field, which is currently dominated by the CRISPR/Cas9 system, requires that the specificity of the DNA manipulation tools should be effortlessly modified to target different genome sequences. However, target specificity of DNA recombinases cannot be easily modified which impedes the use of these enzymes in the genome editing applications. On the other hand, the requirements of the field can be satisfied if the exceptionally high level of target specificity of the tyrosine recombinases is lowered to the acceptable levels while maintaining their genome editing functionality and the absence of the off-target effects. This is possible due to the intrinsic property of the tyrosine recombinases that requires that the specificity of both a recombinase variant and its respective recombining targets have to match. Consequently, even if the relaxed specificity tyrosine recombinase variants are capable of targeting several genome sequences, these variants will not cause any off-target effects in the genome. As such, only one or very few tyrosine recombinase variants will be needed to target various genome sequences of interest. The main goal of the our research was to find the attP-like sequences in the human genome in the vicinity of the beta-globin gene that can be recombined by the relaxed specificity variants of lambda Int. We used the bioinformatics approaches to identify such sequences and showed that they indeed can be successfully used by the lambda Int variants as substrates in bacterial cells. Further research in human cells will determine if these attP-like sequences can be utilized to replace the respective defective sequences in the beta-globin locus of the human genome.

57. Formulation and characterization of pluronic lecithin organogel as an efficient transdermal delivery vehicle of the flavonol fisetin and its potent derivatives. **Anthony Walker**, Jean C. Chamcheu, Khalid A. El Sayed, Tarun K. Mandal. University of Louisiana at Monroe College of Pharmacy, Xavier University of Louisiana College of Pharmacy.

Abstract: The major objective of this study is to prepare topical gel formulations of fisetin, a natural dietary polyphenol and DF21, a more potent synthetic derivative of fisetin, and to characterize their efficacies as safer alternatives for treating cutaneous inflammatory disorders with an emphasis on psoriasis. Recent reports and our preliminary research findings showed that i) topical application of fisetin alleviates psoriasis-like lesions in a 3D full-thickness reconstituted human

skin equivalent model of psoriasis (FTRHSP), ii) fisetin modulates chronic inflammatory conditions, and iii) a novel potent amine substituted derivative of fisetin, DF21, modulates skin cells hyperproliferatory responses (>176-fold) and over 15-fold more mTOR kinase inhibitory activity compared with fisetin in vitro. These formulations are hoped to present an advantage over others with less potential for unwanted, adverse side effects. Pluronic lecithin Organogel (PLO) is a non-pharmacologically active extemporaneous formulation that is non-toxic, non-irritating, non-allergenic and works rapidly with predictable and reproducible effects. PLO has no pharmacological activity within the body as the skin barrier rapidly resumes to its natural state after its use, and it is cosmetically acceptable. The topical route of administration within the body and skin barrier will allow the active ingredient to effectively bypass the oral and gastrointestinal system, eliminating first pass metabolism, bridging bioavailability issues, and avoiding side effects and problems related to the gastrointestinal tract passage. Based on these positive characteristics, we posit that the medicated PLO formulations will provide successful transdermal delivery of the active ingredient across the skin and increase the active ingredient's permeation ability for systemic absorption to maximize local and systemic therapeutic effects.

58. GleIF4A interactions with subcomplex GleIF3b/3g/3i in Giardia. **Zachary Wiggins**, Srinivas Garlapati, Tim Mcmahan. University of Louisiana at Monroe.

Abstract: Giardia lamblia is a flagellated protozoan human parasite that causes gastrointestinal giardiasis in humans and is responsible for many waterborne outbreaks of diarrhea in the United States. Due to the rise of resistant strains against common drugs such as Metronidazole (Flagyl) and its derivatives, a new approach is needed to treat Giardia. A novel area of study is protein synthesis machinery in Giardia, which has significant differences when compared to its mammalian hosts and could serve as a potential target for future drug therapy. Giardia lacks detectable homologs eIF4G, 4B, and 4H, has smaller 80S ribosomes, and an unusually short 5' untranslated region (0-6 nucleotides). eIF4G exists as a complex with cap binding protein eIF4E and RNA helicase eIF4A and is responsible for recruiting the PIC to the 5' end of the mRNA. eIF4B, eIF4H, and eIF4G together are responsible for stimulating eIF4A helicase activity which unwinds hairpin structures within the untranslated region and aids in scanning. In Giardia, the only detectable homologs of eIF4 are GleIF4A and GleIF4E2. Without its stimulating partners and with the lack of a 5' untranslated region containing secondary structures, the role of GleIF4A in translation is largely unknown in Giardia. Current literature shows a novel interaction between GleIF4A and GleIF3i. GleIF3i exists as a subcomplex with GleIF3b and GleIF3g and this subcomplex is involved in nearly every step of translation initiation. The aim of our study was to elucidate what interactions GleIF4A may have with this eIF3 subcomplex and what implications it may have in understanding GleIF4A's function utilizing both in vitro and in vivo assays.

59. Computational methods for development of fusarochromanone as an inhibitor of tyrosyl-DNA phosphodiesterase 1 (TDP1) for cancer treatment. **E'Keria Williams**, Dr. Brian Salvatore, and Dr. Elahe Mahdavian. Louisiana State University Shreveport.

Abstract: Cancer has claimed many lives and compromised the quality of life for billions of people. Despite much progress, there is still a dire need for better cancer therapeutics that are safer and more effective. Recent pre-clinical studies have led to significant interest in fusarochromanone (FC101) as a promising experimental cancer drug. FC101 exhibits poly-pharmacology, strongly

impacting multiple cancer cell phenotypes (proliferation, viability, survival, and migration). This project is based on two important experimental observations. First, FC101 binds with high affinity to tyrosyl-DNA phosphodiesterase (TDP1) protein and inhibits its catalytic function. Thus, TDP1 is a potential target of FC101, and this inhibition may contribute to FC101's mode of action as a cancer drug. Second, while FC101's displays potent in vitro anticancer activity, its performance in in vivo is less impressive. Therefore, we aim to improve FC101's performance in vivo through the rational design of new bioisosteric analogs targeting TDP1. Computer-aided drug discovery (CADD) and applied bioinformatics tools have emerged as reliable predictive tools in drug discovery. We assembled a drug library containing FC101, 18 bioisoteric and 6 medicinal chemistry analogs. This assortment of compounds was designed using medicinal chemistry insights to explore structure/function relationships and structural modifications that improve FC101's anti-cancer activity. We employed molecular docking to assess the binding affinity of the drug candidates to TDP1 (PDB:ID 1qzq) and screened the ADME parameters for each compound, removing analogs with undesirable physiochemical characteristics. This furnished a priority list of compounds for further testing and lead optimization. We have identified three new analogs that possess strong binding affinity and superior drug-like properties, compared to FC101. This has laid the groundwork for the preclinical development of novel FC101 analogs targeting TDP1.

60. Bulk and single-cell transcriptomic profiling to study the neuronal differentiation of mouse ES cells. **Anna Wilson**, Eduardo Martinez-Ceballos. Southern University A&M - Baton Rouge.

Abstract: The ability of embryonic stem cells (ESCs) to differentiate into any cell type of the body presents an opportunity to obtain neuronal progenitors capable of repairing nervous tissues. Specifically, particular studies have focused on generating GABAergic neurons from ESCs as a method to replace damaged neurons due to their ability to release the GABA inhibitory neurotransmitter. In this regard, studies have shown the potential of neural stem cell (NSC) transplantation, but a major drawback of this approach is that NSCs produced from stem cells have the ability to cause allogeneic responses, which can lead to tumor formation due to the heterogeneity of the neuronal populations being produced during culture. Thus, because teratogenesis after transplantation is possible, a better understanding on the molecular mechanism of ESC to GABAergic neuronal differentiation is required. In this regard, we previously reported that mouse ESCs encapsulated in hydrogels and treated with all-trans-retinoid acid (RA) were able to generate GABAergic neurons with high efficiency. However, the molecular mechanism associated with GABAergic differentiation through this differentiation protocol is not well known. To address this, we performed time-series transcriptome analyses on encapsulated vs standard embryoid bodies (EBs) of mouse ESCs treated with RA for two (2D-RA) or four days (4D-RA). Control cells were treated with vehicle only for two days. We found genes differentially expressed in EBs as compared to encapsulated cells. Particularly, Hap1 had decreased expression in EBs from C to 4D-RA but had constant expression in encapsulated C to 4D-RA. We identified a group of genes that were differentially expressed in encapsulated versus non-encapsulated cell cultures and may be responsible for the determination of neuronal fate.

61. Anti-psoriatic and Anti-inflammatory effects of Novel Fisetin Derivatives in Keratinocytes and Macrophages In Vitro. **Rajesh Yadav**, T Roy, ST Boateng, Li H, JT Folahan, MA Mahmud, He H, M Bramwell, S Banang-Mbeumi, Siriki A, S Murru, P Maher, Ma H and JC Chamcheu. University

of Louisiana at Monroe, University of Rhode Island, Salk Institute for Biological Studies.

Abstract: Psoriasis (PS) is a chronic inflammatory skin disease involving skin and immune cells interactions causing hyperplasia and inflammation. Due to the mutifactorial pathogenic attribute, that makes it difficult and expensive to treat even with current FDA-approved biologics, there is a need to develop newer and efficacious PS therapies. Fisetin, a polyphenolic nutraceutical with several beneficial properties like antioxidation, antiproliferative, anti-inflammation, and has been identified with in vitro and in vivo anti-psoriatic effects. Despite fisetin's ability to improve psoriasis-like features, its poor lipid solubility, low bioavailability, and rapid biotransformation limits its usage viz different routes. This study identifies novel fisetin derivatives lacking the susceptible 7-hydroxy or the 3',4'-di-OH group on ring A and B respectively but with enhanced anti-psoriatic and anti-inflammatory properties using fluorometric techniques and in vitro skin(keratinocytes-HaCaT) and immune (macrophages-RAW 264.7) cell culture models. Several of these compounds show better cyclooxygenase-2 (COX 2) inhibitory activity as compared to the parent molecule using COX-2 ELISA assay kit. Nitric oxide levels and cytokines (TNF-α/IL-6) that mediate the inflammation cascade were significantly reduced by the potent derivatives in lipopolysaccharide (LPS) and interferon-gamma(INF-ɣ)-stimulated RAW 264.7. The molecular expression of key signalling pathway markers implicated in PS and other inflammatory disorder such as pAkt, p-mTOR, p-Raptor, p-GSK3β, iNOS and IL-22 were significantly reduce in TNF-α activated HaCaT using western blotting. The level of Ki-67, a hyper-proliferation protein was also significantly reduced in activated-HaCaT treated with derivatives as analyzed by immunostaining. In summary, our data support the anti-inflammatory propensity of these novel fisetin-derivatives, and suggest they could further be developed against psoriasis and others inflammatory conditions.

62. Molecular mechanism of cancer progression inhibited by PI3K inhibitor in prostate cancer. **Xiaoping Yi**, Akajiugo Amucheaz, Eduardo Martinez-Ceballos, Konstantin Kousoulas, and Xiaoping Yi. Department of Biological Sciences and Chemistry, Southern University and A&M College, Division of Biotechnology and Molecular Medicine and Department of Pathobiological Sciences, School of Veterinary Medicine, Louisiana State University.

Abstract: Prostate cancer is the most common cancer in men. Age, diet, gene mutations are associated with increased risk for prostate cancer. However, the cellular processes that are responsible for generation of a cancer cell are not well known, although it is suspected that dysregulation of cellular pathways may be directly or indirectly contributing to prostate cell generation. Activation of the phosphatidylinositol 3-kinase (PI3K) and mammalian target of rapamycin (mTOR) pathway has been strongly linked with prostate cancer progression and metastatic potential. Our hypothesis is that application PI3K/mTOR inhibitor such as BEZ235 cause specific signaling cellular pathways changes leading inhibition of prostate cancer progression. To accomplish this Aim, prostate cancer spheroids (3D cancer cultures) will be treated with inhibitor and the effect of inhibitor on cells under specific pathway inhibition conditions will be examined at the transcriptomic and proteomic levels. Our results showed that inhibitor inactivation of AKT phosphorylation, downregulation of expression of the AKT but not affected the expression of PI3K and mTOR, and then affected cell cycle arrest in G0/G1 phase, activation of IAP1/2 to inhibition the tumor progression. The results obtained from this project will help us

understand the role of inhibitor on prostate cancer progression and will provide an insight on mechanisms of chemotherapy resistance.

Core Structure and Committees

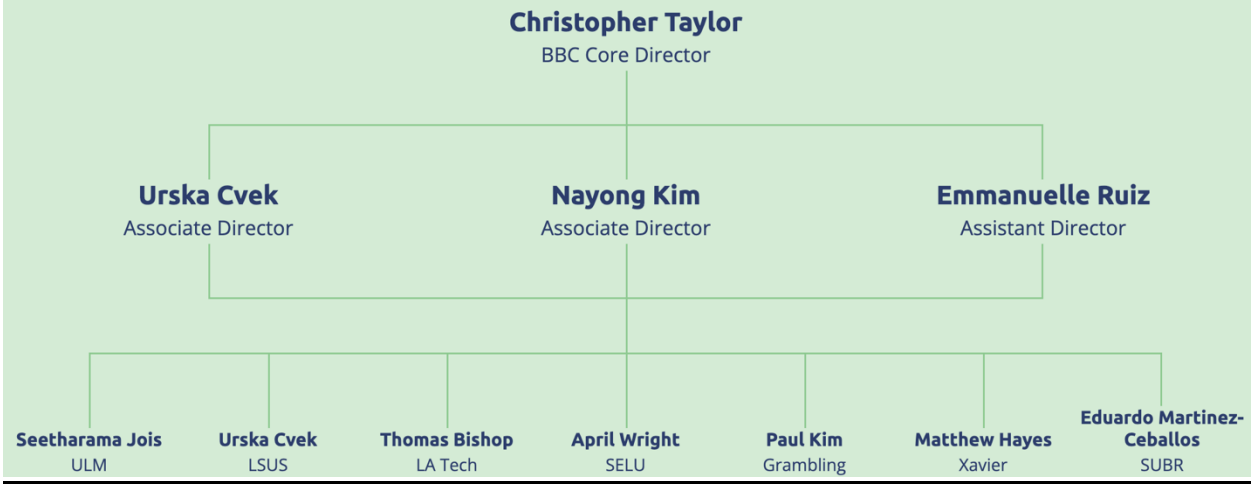
Administrative Core

The Administrative Core (AC) of the Louisiana Biomedical Research Network (LBRN) provides the project with its overall leadership, day-to-day management, evaluation of all of its component parts, and communication with NIH staff. The AC is led by the Principal Investigator in close consultation with the Program Coordinator, as well as the Steering Committee and External Advisory Committee.

Core Structure and Committees

Bioinformatics, Biostatistics, and Computational Biology Core

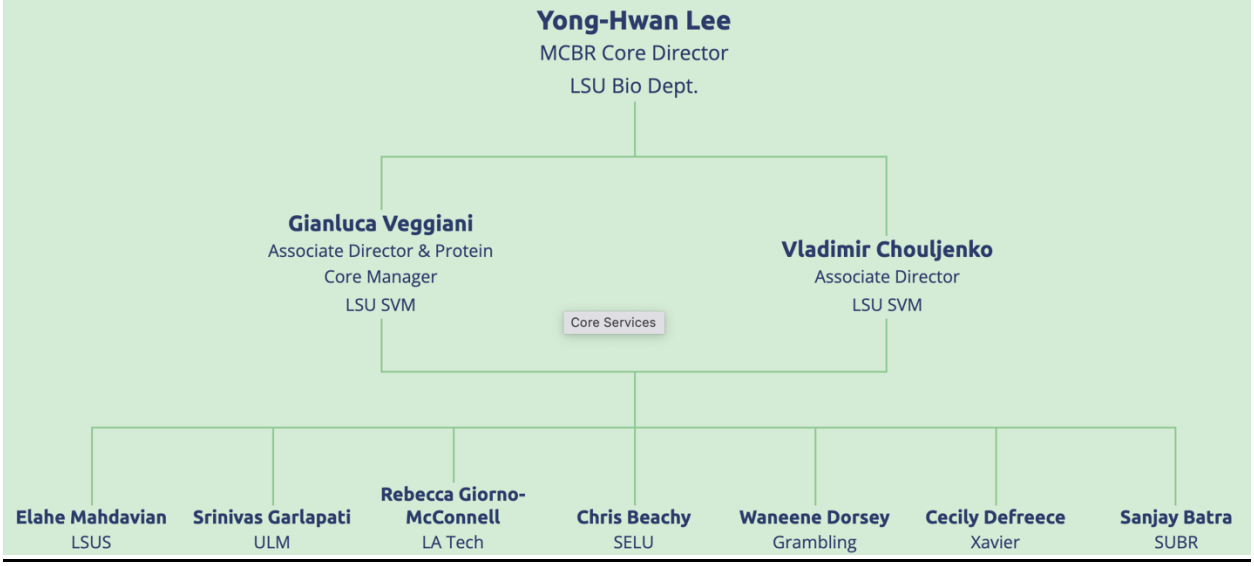
The Bioinformatics, Biostatistics, and Computational Biology Core (BBCC) of the Louisiana Biomedical Research Network (LBRN) serves to train and support project investigators and their teams across Louisiana, and to lead and support translational research activities at the frontiers of biomedical science. Its team uses both established and custom computational tools, operating at computational scales ranging from the mundane to analyses engaging many hundreds of compute cores.



Core Structure and Committees

Molecular and Cell Biology Resources Core

Molecular and cell biology provide an essential linkage among important basic fields of biomedical science, such as genetics, developmental biology, structural biology, immunology, neurobiology, and cancer biology. The MCBRC takes advantage of existing highly organized, centralized services and equipment facilities located primarily at the LSU flagship institution in Baton Rouge, effectively uniting these units toward the common goal of supporting biomedical research performed by PUI investigators. The MCBRC will provide technical and logistical support, enabling the ready exchange of information, ideas, technology, and research capabilities among PUI investigators. MCBRC will ensure that PUI researchers have full access to state-of-the-art equipment and modern research techniques and services.



Core Structure and Committees

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