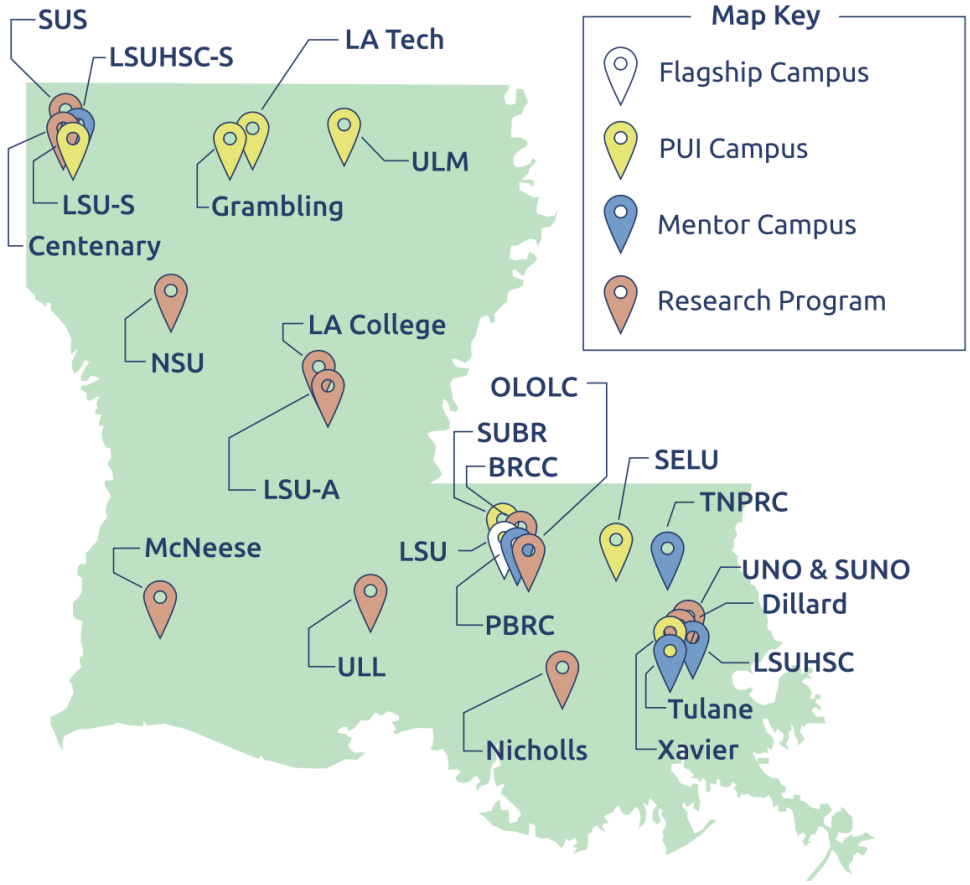
LBRN

Louisiana Biomedical Research Network



Louisiana Biomedical Research Network
18th Annual Meeting
January 17 – 18, 2020

Louisiana State University
Union Theater
Baton Rouge, LA

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LBRN 18th Annual Meeting
Louisiana State University
Student Union
Baton Rouge, LA
January 17-18, 2020

FRIDAY, JANUARY 17, 2020			
Time Begin	**Time Ends**	**Location**	**Event**
12:00 PM	Open	Atrium	**Registration (Poster and Conference)**
1:00 PM	1:15 PM	Theater	*Opening Remarks*
1:15 PM	3:00 PM	Theater	Louisiana IDeA Program PIs
3:00 PM	3:15 PM	Atrium	**BREAK (Refreshments)**
3:15 PM	3:30 PM	Theater	COBRE/LBRN Pilot:JCC/SP
3:30 PM	3:45 PM	Theater	Seetharama Jois
3:45 PM	4:00 PM	Theater	David Mills
4:00 PM	4:15 PM	Theater	Jamie Newman
4:15 PM	4:30 PM	Theater	Urska Cvek
4:30 PM	4:45 PM	Atrium	**BREAK (Refreshments)**
4:45 PM	5:15 PM	Theater	**Graduate Student Flash Talks**
5:30 PM	6:30 PM	Royal Cotillion Ballroom	**Poster Session**
6:30 PM	8:30 PM	Royal Cotillion Ballroom	**Dinner and Posters**

SATURDAY, JANUARY 18, 2020			
Time Begin	**Time Ends**	**Location**	**Event**
7:30 AM	Open	Theater	***Registration (Conference)***
8:15 AM	8:30 AM	Theater	***Introduction***
8:30 AM	9:30 AM	Theater	**Dr. Augusto Ochoa, Dir. LCRC**
9:30 AM	9:45 AM	Theater	Dr. Siva Murru
9:45 AM	10:00 AM	Theater	Dr. Vonny Salim
10:00 AM	10:15 AM	Atrium	**Break (Refreshments)**
10:15 AM	10:30 AM	Theater	Dr. Rami Al-Horani
10:30 AM	10:45 AM	Theater	Dr. Georgio Matthaiolampakis
10:45 AM	11:00 AM	Theater	Dr. Devaiah Kambiranda
11:00 AM	11:15 AM	Theater	**Dr. Garlapati Srinivas**
11:15 AM	11:30 AM	Theater	**Dr. April Wright**
11:30 AM	12:00 PM	Theater	**Dr. Xiaoping Yi**
12:00 PM	1:00 PM	Royal Cotillion Ballroom	**LUNCH**
1:00 PM	1:30 PM	Theater	**Dr. Paul Kim**
1:30 PM	2:00 PM	Theater	**Dr. Anup Kundu**
2:00 PM	2:30 PM	Theater	**Dr. Karen Zhang**
2:30 PM	3:00 PM	Theater	**Break (Refreshments)**
3:00 PM	3:15 PM	Theater	**Dr. William Yu**
3:15 PM	3:45 PM	Theater	**Dr. Waneene Dorsey**
3:45 PM	4:15 PM	Atrium	**BREAK (Refreshments)**
4:15 PM	4:30 PM	Theater	**AWARDS**
4:30 PM	5:30 PM	TBD	EAC, SC, Core Directors, & Admin Mtg

Meeting Hotel
Courtyard Baton Rouge Acadian Center/LSU
2421 South Acadian Thruway
Baton Rouge, LA 70808

Abstracts for Oral Presentations by Faculty & Graduate Students

Oral Presentation Abstracts

	3:15 PM - 3:30 PM | Friday
	Role of mTOR and its targeting by fisetin for treating psoriasis
	Dr. Jean Christopher Chamcheu, Sonika Patial
	University of Louisiana at Monroe, LSU School of Veterinary Medicine
	Treatment for psoriasis, a chronic inflammatory skin disease remains elusive. Aberrant activation of the mTOR signaling cascades have emerged as relevant molecular targets for psoriasis. Therefore, developing natural agents or their synthetic scaffolds that can inhibit their activation could be of potential clinical benefit to psoriasis patients. Our earlier studies identified fisetin, a natural dietary 3',4',7 trihydroxyflavonol, as a potent mTOR/p70S6K kinase inhibitor (Biochem Pharmacol.;89(3):349-60.), and recently showed it attenuates psoriasis-like features in vitro in activated epidermal keratinocytes and immune cells (Cells. 2019 Sep 15;8(9). pii: E1089.). Here, we studied the effect of fisetin in-vivo using an imiquimod (IMQ)-induced psoriasiform disease model in Balb/c mice, and begun generating a myeloid lineage mTOR knockout mouse model to validate the concept. Topical application of IMQ cream induced mouse psoriasis-like skin lesions characterized by increased erythema, ear swelling (acanthosis and hyperkeratosis), and scaling. Moreover, immunohistopathological analysis revealed the activation of Akt/mTOR pathway compared to matched control tissues. Lesional skin tissue sections of mice topically treated with fisetin (1mg/cm2 of shaved skin/ear, daily) exhibited significant decrease in i) psoriasiform hyperplasia including ear swelling and epidermal thicknesses, ii) erythema, iii) levels of inflammatory mediator and cytokines (IL-22 and iNOS) and iv) proliferation (Ki-67) when compared with control mice. Furthermore, fisetin-treated lesioned skin sections showed decreased Akt and mTOR phosphorylation. To confirm the role of mTOR in psoriasis, we are currently generating myeloid-cell specific mTOR deficient mice for use in asserting the role of fisetin as mTOR inhibitor for treating psoriasis. Validating these in myeloid cell lineage mTOR deficient mice will provide useful translational data that could potentially benefit psoriasis management and other hyperproliferative skin diseases. Taken together, our data affirm the involvement of mTOR in psoriasis, and suggest fisetin as a useful inhibitor to be developed.
	3:30 PM - 3:45 PM | Friday
	Grafted peptidomimetics for immunomodulation
	Dr. Seetharama Jois, Achyut Dahal, Konstantin G Kousoulas
	University of Louisiana at Monroe, Louisiana State University
	The long-term goal of this project is to understand the protein-protein interactions (PPI) of cell surface molecules and inhibit these PPI to modulate cell signaling in the inflammatory response using novel stable peptide molecules. Naturally occurring cyclic peptides such as sunflower trypsin inhibitor (SFTI) with disulfide bonds are resistant to thermal, chemical, and enzymatic degradation. The objective is to use the SFTI template to design stable peptide molecules to modulate the PPI of CD2-CD58 (CD48 in mice) adhesion/costimulatory molecular interactions. Blocking of CD2-CD58 molecules interactions results in inhibiting co-stimulatory signals required for the generation of the immune response that ensures the production of pro-inflammatory cytokines and inflammation. Peptides from CD2 protein have been designed to block CD2-CD58 interactions in an in vitro model system of T cells and epithelial cells. A newly grafted peptidomimetic (SFTI-DBF) from the SFTI template has recently been

	generated to inhibit PPI of CD2-CD58 interactions. The peptidomimetic exhibited cell adhesion inhibition activity between T-cells and HFLA-RA cells with an IC50 value of 3 nM. To evaluate the ability of SFTI-DBF to bind to CD58 protein, surface plasmon resonance analysis was carried out. SFTI-DBF showed binding to CD58 with a Kd value of 46 nM. Competitive binding of SFTI-DBF with FTIC-AbCD58 indicated that the peptidomimetic binds to CD58 on the adhesion domain. Furthermore, the ability of SFTI-DBF to inhibit protein-protein interaction of CD2-CD58 was evaluated by proximity ligation assay. SFTI-DBF is shown to inhibit PPI of CD2-CD58 in a concentration-dependent manner. The peptidomimetic was able to decrease the calcium flux in T cells indicating the ability of SFTI-DBF to modulate the T- cell mediated immune response. Stability study of SFTI-DBF under different conditions indicated that it was stable against trypsin digestion and thermal degradation.
	3:45 PM - 4:00 PM | Friday
	3D Printed Nanoclay Enhanced Ceramic Composite for Bone Regeneration
	Dr. David Mills, Anusha Elumalai, Jennifer Woerner
	Louisiana Tech University, LSU Health Science Center Shreveport
	Craniomaxillofacial (CMF) surgeons treat bone defects using autografts, allografts, and even xenografts in an attempt to restore functionality and aesthetic appearance. Metallic biomaterials are bioinert, possess little biological activity in vivo, with subsequent poor tissue integration, increased incidence of inflammation and infection, and implant loosening and failure due to infection. A more attractive solution is to fabricate a customized drug-eluting and biodegradable implant (e.g., resorbable bone mesh, screws and plates) using 3D printing technology. Our polymer nanocomposite will couple the treatment of infection while simultaneously encouraging tissue regeneration. The nanocomposite will consist of a polycaprolactone (PCL) and polyethylene oxide (PEO) polymer blend, and a calcium phosphate cement (CPC) enhanced with halloysite nanotubes (HNTs). The PCL/PEO blend will have controlled degradation and will be coupled with HNTs doped with antimicrobials and osteoinductive/osteogenic growth factors (hereafter termed bioactive agents). It can also serve as an orthobiologic. When applied or implanted into bone tissue, it will facilitate disease remediation, osteogenesis, matrix formation, mineralization, and biointegration. This project will produce novel, cost-effective and customizable medical devices for use in the treatment of developmental or traumatic CMF defects or injuries.
	4:00 PM - 4:15 PM | Friday
	Comparing Treatment of Adipose Stem Cells for the Differentiation of Clinically Relevant Cells
	Dr. Jamie Newman, Bruce Bunnell, Mary Caldorera-Moore, Jeff Gimble
	Louisiana Tech University, Tulane University
	Human adipose-derived stem cells are the easiest adult stem cells to access, harvest, and isolate, providing the largest supply of autologous stem cells for clinical application. As stem cells, hASCs have the ability to self-renew, differentiate, and suppress inflammation. These cells are being used along with

Oral Presentation Abstracts

	other components of the stromal vascular fraction (SVF) to treat autoimmune conditions, inflammatory diseases, and specific injuries. In clinical trials, these cells are being isolated and expanded to treat a similar set of health conditions with a more targeted interest in regeneration. With the interest in using isolated stem cells in cell-based treatments and in areas of tissue engineering and regenerative medicine it is critical that we find efficient and clinically relevant methods for maintaining and differentiating stem cells. To work towards creating cells that can be reliably used in the clinic and generate functional myogenic tissue we are assessing conditions of hASCs culture in physiologically relevant environments and assessing the influence of physiologically relevant environment on cellular memory. This understanding will aid in the development of clinically relevant methods to overcome limitations currently presented for long-term culture and therapeutic use of adipose-derived stem cells. Myogenic differentiation will be assessed by examining cell morphology and expression of myogenic markers under each of the culture conditions.
	4:15 PM - 4:30 PM | Friday
	Establishing a Protocol for Activating the Massive Transfusion Protocol for Air Medical Service Trauma Patients
	Dr. Urska Cvek, Phillip C.S.R. Kilgore, Brian Cornelius, Angela Cornelius
	Louisiana State University Shreveport, LSU Health Sciences Shreveport, Ochsner LSU Health Shreveport
	Trauma is the leading cause of death world-wide in persons under the age of 40 and accounts for approximately 10% of all deaths in general. Massive hemorrhage is a major cause of early death in trauma patients in both civilian and military trauma care. In the initial management of trauma patients both interventions in hemostasis and proper preparation of blood products are crucial to prevent hemorrhagic shock, which can easily lead to early death. Massive Transfusion Protocols (MTPs) are initiated after established policies in many trauma centers, but too many centers still rely heavily on subjective clinical judgment of patient's initial vital signs. As familiarity with MTP triggers has increased, there is a growing interest and need in applying these in the civilian and military populations to initiate them earlier and to identify easy and fast ways to predict the need for MTP. Triggers have differential predictive values for the need of transfusion, and defining the utility of each criterion will help to identify those most likely to benefit from an early initiation of the MTP. We made preliminary investigations of previously published studies of MTP protocols and determined that many of them are very complex and require variables that are not available until trauma arrival and are thus not usable for air medical service. Previous studies have not revealed a single measurement of vital signs that are a good predictor in determining the need for MTP activation. For this reason, we are interested in identifying a reliable and easy-to-calculate MTP trigger. Our goals are to (1) evaluate the reliability of air medical blood product transfusion as a trigger for MTP, (2) determine the reliability of air medical calculation of Shock Index (SI) as a trigger for MTP and (3) identify a rapid and simple scoring system for MTP based on a comparison across existing scoring systems. We present preliminary results of our translational project.

Oral Presentation Abstracts

	9:30 AM - 9:45 AM | Saturday
	Design, Synthesis and Evaluation of Pyrazole Derivatives as Potential Anti-Cancer Agents
	Dr. Siva Murru, Seetharama Jois, George Stanley
	University of Louisiana at Monroe, Louisiana State University
	Nitrogen heterocyclic compounds are an integral part of a huge number of natural and synthetic compounds and play important roles in the biological systems. Among those, pyrazole derivatives can be fine-tuned to achieve desired electronic and steric effects, essential features required for the desired biological activity. Currently we are working on synthesis and biological evaluation of pyrazole and pyrazolone based small molecules as potential anticancer agents. We have recently identified a set of compounds exhibiting anticancer activity particularly towards non-small cell lung cancers (NSCLC). Until now, treatment of NSCLC has had limited success and new therapeutics are desperately needed. We have synthesized several derivatives of lead molecule(s) and the preliminary in-vitro antiproliferation using Celltiter Glo assay have shown a few compounds with good potency against two cancer cell lines i.e. human lung carcinoma (A549) and human adenocarcinoma (NCI H522). In addition to that, we performed PARP inhibitor analysis and cell cycle analysis, and obtained data from kinase profiling studies. We will present the data and results from our synthetic approaches and biological assays.
	9:45 AM - 10:00 AM | Saturday
	Elucidation of Anticancer Camptothecin Biosynthetic Pathway for Metabolic Engineering and Drug Discovery
	Dr. Vonny Salim, Urska Cvek, Elahe Mahdavian, Xiuping Yu, Hugh Nam, Khalid El-Sayed, Daniel A. Jones, Dean DellaPenna
	Louisiana State University - Shreveport, Louisiana State University Shreveport, Louisiana State University Health Sciences Center, University of Louisiana at Monroe, Michigan State University
	Monoterpene indole alkaloids (MIAs) occur in a very diverse plant families and become the source of several pharmacologically active compounds, including those are anticancer drugs, such as camptothecin and Vinca alkaloids. While these drugs have been widely used in chemotherapy treatments, their productions still rely on extraction from the medicinal plants Camptotheca acuminata and Catharanthus roseus. In addition, these compounds are present in minute amounts in the plants as a result of intricate metabolic pathways. Large scale sequencing of these important medicinal plants has allowed the availability of transcriptomes and genomes for identification of genes involved in MIA biosynthetic pathways. Here, we biochemically characterize genes involved in camptothecin biosynthesis for developing microbial systems to manufacture the bioactive MIAs. Recent elucidation of glucosidases involved in camptothecin biosynthesis reveals the complexity of MIA pathways in C. acuminata, which differ significantly from alkaloid strictosidine glucosidase from C. roseus. While C. roseus glucosidase prefers its native substrate 21(S)-strictosidine, C. acuminata glucosidases are active toward multiple isomers of alkaloid intermediates in camptothecin pathway with varying affinities. Functional characterization of these diastereo-active glucosidases from C. acuminata offers significant enzymatic and kinetic insights into the anticancer camptothecin biosynthetic pathway for application in

	enzyme engineering efforts and further characterization of other camptothecin biosynthetic genes. A vast chemical diversity with substantial pharmacophores displayed by MIAs will also inspire metabolic engineering approaches and more anticancer drug discovery.
	10:15 AM - 10:30 AM | Saturday
	Inhibition of FXIIIa by Sulfonated Molecules as Potential Avenue to Novel Anticoagulants
	Dr. Rami Al-Horani, Mentor: Dr. Rinku Majumder
	Xavier University of Louisiana, LSU Health Science Center
	Purpose. Thrombosis remains a major public health crisis. Current treatment entails the use of anticoagulants which, despite their efficacy, are associated with significant bleeding. Thus, new approaches to safely treat thrombosis are needed. Factor XIIIa (FXIIIa) is a transglutaminase that catalyzes the last step in the coagulation process. Interestingly, venous thrombi from FXIII-deficient mice were significantly small. Studies also revealed that specific FXIIIa polymorphism protects against venous thrombosis and that heterozygous FXIII-deficient mice do not suffer from excessive bleeding. Thus, FXIIIa has been targeted to develop new anticoagulants with minimal bleeding. Few orthosteric FXIIIa inhibitors were reported, yet none was selective. We have proposed to develop allosteric inhibitors so as to achieve selectivity. Methods. A library of sulfonated molecules was screened for FXIIIa inhibition in a transglutamination assay. The effect on fibrin polymerization as well as the inhibition mechanism and selectivity were evaluated. Cellular toxicity was assessed using a proliferation assay. Molecular modeling was exploited to determine the inhibitors' putative binding site. Results. Four molecules inhibited FXIIIa with IC50 of <5 μM. The inhibitors also affected fibrin polymerization. Michaelis-Menten kinetics revealed a mixed mechanism of inhibition. The best inhibitor was >200-fold selective over thrombin and factor Xa and 8-fold selective over tissue transglutaminase-2. It doubled the clotting times of human plasma but only at concentrations >700 μM. It did not affect the proliferation of three cell lines at 10 μM. Molecular modeling indicated that inhibition of FXIIIa may stem from binding to an anion-binding site involving K73, R68, K61, R56, & K54. Conclusion. The study reports two potent and potentially nonactive site inhibitors of FXIIIa belonging to two chemotypes. The inhibitors will be used in future efforts to develop effective and safer anticoagulants.
	10:30 AM - 10:45PM | Saturday
	miRNA-30a's macrophage activity in Lung Cancer
	Dr. Georgios Matthaiolampakis
	University of Louisiana at Monroe
	Lung cancer (LC) is the leading cause of cancer deaths in the United States and worldwide, with a dismal 5-year survival rate of <15%. The limited therapeutic options currently available for treating LC demonstrate the urgency for novel therapeutic approaches. A developing hypothesis concerning the lack of efficacy of LC drugs is that these drugs primarily target tumor cells, while ignoring the tumor microenvironment. As part of the tumor microenvironment, Tumor Associated Macrophages (TAMs)

	can promote or inhibit tumor growth and metastasis, depending on their inflammatory responses. During LC progression, TAMs switch to anti-inflammatory-like phenotype increasing fibroblastic morphology, promoting tumor cell proliferation and migration, which correlates to poor prognosis. Small non-coding RNAs, such as microRNAs (miRs), are recognized as crucial post transcriptional regulators of gene expression with significant therapeutic potential in regulating tumor growth. Multiple miRs have been recognized as tumor suppressors or oncogenic, and clinical trials are undergoing to identify their therapeutic potential for cancer treatment. miR-30a has been established as a strong tumor-suppressing nucleic acid against LC. Yet, no knowledge exists of its activity on TAMs. Such significant knowledge can impact its potential clinical translation, our perspective on using miR-30a for treatment of LC and other types of cancer, and will provide with important insight for appropriate drug combinations. Although the miR-30a is recognized as a tumor suppressor for LC, the miR also affects the expression of genes associated with macrophage polarization, such as iNOS and Arginase-1. Our progress indicates the miR-30a does effect macrophage polarization, favoring an anti-inflammatory responses. We continue on this work for identifying potential mechanistic targets and the behaviour of this miR in additional cell lines, such a human U937 monocytes.
	10:45 AM - 11:00 AM | Saturday
	Anti-inflammatory Effects of Ellagitannin Metabolites in E-cigarette Vapor Condensate
	Dr. Devaiah Kambiranda, Rizwana Begum, Sanjay Batra
	Southern University and A&M College, Southern University and A&M College
	E-cigarettes (e-cigs) are battery-operated heating devices which convert e-cigarette liquid (e- liquid) into an inhalable vapor. Since their introduction in the United States (US) markets in 2007, e-cigs have become popular amongst people of all ages. Toxicological assessment of e- cigs and aerosols by the United States Food and Drug Administration and independent researchers demonstrate that emissions from e-cigs contain propylene glycol, heavy metals and other carcinogens in the form of nanoparticles. Moreover, the vapors from flavored e-liquids have been shown to induce greater stress and toxicity on the lung tissue as compared to those from non-flavored e-liquids. There have also been reports of bronchiolitis, acute eosinophilic pneumonia, inhalation injury, and suspected acute hypersensitivity pneumonitis associated with e-cigs use. Our results show significant increase in cytokines/chemokines by tobacco flavored e-cigs vapor condensate (TF-ECVC)-challenged alveolar lung epithelial cells as compared to filtered air-exposed cells. We also found noticeable increase in the expression of inducible proteasome subunits in TF-ECVC-challenged cells. Furthermore, we tested our hypothesis if ellagitannin metabolites Urolithin A (Uro-A) and Urolithin C (Uro-C) can combat with TF-ECVC induced inflammatory responses and dysregulated constitutive/inducible proteasome machinery in A549 cells. Overall, our results demonstrate that Uro-A and Uro-C possess significant potential to mitigate vaping induced inflammation and dysregulated protein homeostasis mechanisms.

Oral Presentation Abstracts

	11:00 AM - 11:15 AM | Saturday
	Mechanism of Translation Initiation in the Protozoan parasite Giardia lamblia
	Dr. Srinivas Garlapati
	University of Louisiana at Monroe
	Translation initiation factor eIF4F is essential for cap-dependent translation initiation in eukaryotes. eIF4F is a trimeric complex consisting of a scaffold protein eIF4G, cap-binding protein eIF4E and DEAD-box RNA helicase eIF4A. eIF4F binds to the 5' cap structure of the mRNA through eIF4E and facilitates the binding of the preinitiation complex (PIC) via protein-protein interactions of eIF4G with eIF3 in mammals or with eIF5 in yeast. In Giardia, homologs for eIF4E (GleIF4E2) and eIF4A (GleIF4A) have been identified but not for eIF4G. To address how PIC is recruited to the 5' end of the mRNA in the absence of eIF4G homolog, we have used yeast two-hybrid assays to identify potential interactions of GleIF4E2 with the components of the PIC. The results show that GleIF4E2 can interact with the beta subunit of the initiation factor GleIF2, a `component of the PIC. ZDOCK modeling of the GleIF4E2-GleIF2 complex revealed that the dorsal side of GleIF4E2 is likely involved in binding to GleIF2. Site-directed mutagenesis of the ZDOCK predicted residues of GleIF4E2 disrupted of its interaction with GleIF2. These results suggest that GleIF4E2 can facilitate the recruitment of the PIC to the 5'end of the mRNA by interacting directly with PIC. The role of GleIF4A in translation initiation in Giardia is not clearly understood. Interestingly, Pateamine A, a specific inhibitor of human eIF4A, inhibited the growth of Giardia in a dose-dependent manner, suggesting that the activity of GleIF4A is probably required for translation. Using yeast two-hybrid assays, we have identified a novel interaction of GleIF4A with i subunit of the initiation factor GleIF3 (GleIF3i), another component of the PIC. Site-directed mutagenesis of ZDOCK predicted residues in N-terminal domain of GleIF4A disrupted its interaction with GleIF3i. These results indicate that the GleIF4A can also interact directly with the components of the PIC.
	11:15 AM - 11:30 AM | Saturday
	Incorporating Heterogenous Data Sources in Phylogenetic Modeling
	Dr. April Wright, Jeremy Brown
	Southeastern Louisiana University, Louisiana State University
	Biomedical research is in the midst of a data revolution. Most scientists now are familiar with the term "big data." However, big data are not the only sources of challenge for modern scientists. Heterogeneous data, or data originating from multiple sources, also poses interesting scientific and training problems for researchers. In this talk, I will discuss work in my laboratory on estimating phylogenetic data from heterogeneous data sources. In particular, we work with models for integrating genetic, phenotypic, and occurrence time data. Confronting the challenges of working with multiple data types within one phylogenetic analysis has required my lab group to propose new analytical models, new metrics for understanding how well our models are performing, and implementing new training programs to onboard students into research.

Oral Presentation Abstracts

	11:30 AM - 12:00 PM | Saturday
	Inhibition of molecular pathways by resveratrol in 3D cell cultures of prostate cancer cells
	Dr. Xiaoping Yi, Eduardo Martinez-Ceballos, Konstantin Kousoulas
	Southern University and A&M College, LSU School of Veterinary Medicine
	Prostate cancer is the most common cancer among American men. Researchers do not know exactly what causes prostate cancer but, on a basic level, prostate cancer is caused by changes in the DNA of a normal prostate cell. Although new treatments for prostate cancer continue to be investigated, no definitive cure has been found yet for the advanced aggressive stages. Resveratrol (RES) is a component of Asian traditional medicine used to treat cardiovascular diseases. Recently, RES has gained considerable attention as an anticancer agent potential use in chemoprevention and chemotherapy for various cancer forms relies on its effects on cell growth, apoptosis, angiogenesis, and cancer metastasis. As RES appears to have many anti-tumor effects on different cancer cell types, the molecular basis of these effects needs to be extensively studied using a cell culture model that best resembles the tumor environment in the body. To identify RES target genes involved in the activation of cell apoptotic pathways, we exposed DU145 cells to different concentrations of RES and performed transcriptome analyses by proteome profiler. There were 16 proteins (such as Bcl-2,Bcl-x, cIAP1 and 2, xIAP) down-regulated at least twofold (P. <0.05) in response to RES and 4 proteins(such as Pro-Caspase-3 , p21, SMAC/Diablo, HSP60) up- regulated in 3D cell cultures of prostate cancer cells by analysis of human apoptosis array. Further analysis by human XL oncology array, there were 22 proteins down-regulated at least twofold (P. <0.05) in response to RES. Under-expression of anti-apoptotic genes and over-expression of pro-apoptotic genes can result in the increase of cancel cell death. Inhibition of oncology genes enhances the effects of apoptotic signals and causes signaling mechanism-based killing of cells in prostate cancer cells. These will allow us to better understand RES mechanism of action and its potential use as a coadjuvant drug for established cancer treatments.
	1:00 PM - 1:30 PM | Saturday
	A visit to the ER: stress, inflammation, and disease
	Dr. Paul Kim, Jacqueline Stephens
	Grambling State University, Pennington Biomedical Research Center
	Various insults including high-saturated fat diet can induce endoplasmic reticulum (ER) stress and activate the unfolded protein response (UPR), which in turn mediate inflammation and contribute to disease. How saturated fats induce ER stress is not clearly understood however. We investigated three potential mechanisms related to protein homeostasis and present data suggesting that saturated fats impair protein folding by dysregulating intracellular calcium signaling. Chronic inflammation appears to be a unifying factor in many diseases. Mitogen-activated protein kinase-activated protein kinase 2 (MAPKAPK2) or MK2 is a downstream effector of the MAPK family member p38. The p38-MK2 signaling axis is well known to regulate the inflammatory response, thus it is an important target of anti-inflammatory drugs. We explore the use of cell penetrating peptides to deliver an MK2 inhibitor across the plasma membrane barrier.

Oral Presentation Abstracts

	1:30 PM - 2:00 PM | Saturday
	Targeted Delivery of Doxorubicin Liposomes for Her-2 Positive Breast Cancer Treatment
	Dr. Anup Kundu, Nusrat Chowdhury, George Olverson, Shanzay Chaudhry, Nicholas Hall, Tarun Mandal, Srikanta Dash, Qian-Jin Zhang
	Xavier University of Louisiana, Tulane University Health Sciences Center
	Doxorubicin is one of the most potent drugs used widely for breast cancer treatment. The adverse side effects and toxicity caused by the non-targeted delivery of doxorubicin has emphasized the demand of emerging a targeted delivery system. The goal of this study is to enhance the delivery of doxorubicin by formulating an aptamer-labeled liposomal nanoparticle delivery system that will carry and deliver doxorubicin specifically into Her-2+ breast cancer cells. Methods: 12 liposomal batches were prepared using different saturated and unsaturated lipids such as DOPC, DPPC, POPC and HSPC by thin film hydration. The liposomes were characterized for particle size and zeta potential. Ammonium sulphate gradient method was used to passively load DOX into the liposomes. Scanning electron microscopy (SEM) was used to investigate the morphology of liposomes. In vitro cytotoxicity assay was done to evaluate the effect of DOX and DOX loaded liposome on MCF-7 and SKBR-3 breast cancer cells. Uptake studies were done with batches F1, F5, F8 and F12 by fluorescence microscopy and flow cytometry. Results: The formulations, F1 through F12, had a small particle size of less than 200 nm and a high entrapment efficiency of about 88±5%. The best formulation, F5, had a particle size of 101±14 nm, zeta potential of +5.63±0.46 mV and entrapment efficiency of ≈93%. The cytotoxicity studies show that the DOX loaded liposomal formulations are more effective in killing cancer cells than the free DOX in both MCF-7 and SKBR-3 cells. The uptake studies show a significant increase in the uptake of the aptamer-labeled liposomes (i.e. F5) by more than 60% into Her-2+ MCF-7 and SKBR-3 breast cancer cells compare to non-aptamer labeled nanoparticles.Conclusion: Aptamer targeted approach results in substantial reduction in the dose of DOX and improves the therapeutic benefits by promoting the target specificity.
	2:00 PM - 2:30 PM | Saturday
	Detecting Race-Relevant Molecular Biomarkers with Clinical Utilities Using Multi-Omics Data Across Tumor Types
	Dr. Kun Zhang, Wensheng Zhang, Zhong Chen, Erik Flemington
	Xavier University of Louisiana, Tulane
	To date, significant progress has been made in our understanding of the role of socioeconomic factors in cancer racial disparities. Increasing evidence now suggests that a number of intrinsic molecular factors specific to malignant cells must also partly account for the observed health inequalities in cancer. Although research has begun to explore the biological basis of cancer disparities, most existing work is limited to several common cancer types and does not methodically explore whether the observed genetic and molecular differences represent the clinically-meaningful racial disparities in other fatal human cancers. Moreover, massive amounts of multi-faceted omics data generated by high-throughput technologies have not been fully utilized and well integrated with clinical data to search for race-

	specific molecular characteristics, biomarkers or potential drug targets. The goal of this LBRN project is therefore to address these limitations by performing a data-driven, pan-cancer study to investigate the cancer-specific molecular differences in different racial groups. The proposed study will focus on the eight TCGA cancer types, with pertinent cancer data from other sources being utilized for methodology development and/or empirical validation throughout the entire project. For a specific cancer, in connection with clinical data, we will develop new bioinformatics algorithms and pipelines to analyze these multi-type omics data individually. As such, we will establish a pan-cancer, race-relevant assemblage of signatures characterized by coherent genes, modules and biological pathways, some of which will hold significance and promise for clinical use. A set of novel analytical tools for the proposed data-driven analyses of cancer disparities will also be developed as open source software. Key results from some recent manuscripts and publications will be discussed in the presentation.
	3:00 PM - 3:15 PM | Saturday
	Enhanced Fluorescent Nanoclusters for Medical Imaging and Sensing
	Dr. William Yu
	Louisiana State University Shreveport
	Small metal nanoclusters (< 2 nm) have superior biocompatibility, tunable emission, large Stokes shift, and long fluorescence lifetime, but low quantum yield. We developed hybridized hierarchical nanostructures that contains big metal nanoparticles (~20 nm) and small metal nanoclusters to greatly enhance the fluorescence emission of the small metal nanoclusters by coupling surface plasmon resonance of the big metal nanoparticles. They are successfully used in imaging and sensing applications.
	3:15 PM - 3:45 PM | Saturday
	Evidence of Inflammatory Responses In Lung A549 Alveolar Epithelial and Human Liver Carcinoma HEPG2 Cells Exposed to Pentachlorophenol
	Dr. Waneene Dorsey, Sanjay Batra
	Grambling State University, Southern University and A&M College, Baton Rouge, LA
	Cumulative studies have shown that organochlorine pesticide exposure aggravates the immune system and augments proinflammatory cytokine activity. Pentachlorophenol (PCP), a restricted-use organochlorine pesticide, is globally known for its agricultural, domestic, and industrial applications. In particular, PCP's fungicidal action against fungal rot and wood-boring insects is largely seen in the treatment of wood and timber products. The carbon-chlorine bond in PCP is resilient to chemical degradation, thus causing it to become persistent in the environment. The United States Environmental Protection Agency has established PCP as an emerging environmental toxicant and Group B2 carcinogen. Avenues of human exposure to PCP-toxicity include the ingestion of food and water, dermal contact, and vapor inhalation. However, the literature is infrequent about the molecular mechanisms affected by acute PCP-toxicity. In this study, we hypothesized that PCP exposure to lung adenocarcinoma epithelial A549-cells characteristics and human liver carcinoma-HepG2 cells would

	result in inflammatory responses. Further, we exposed our mammalian cell lines to varying concentrations (1-10uM) of PCP for 24-hr duration and studied the transcriptional and translational expression of proteins involved in immune and inflammatory responses. At the transcriptional and protein levels, we observed an increased in IL-1β, IL-8, CCL2, and CCL5 in A549 and HepG2 cells. Previous studies have shown that p38/mitogen-activated protein kinase (MAPK) work in concert with NF-kB to transactivate proinflammatory cytokine activity. Data obtained from this study demonstrated an increase in the expression of transcription factor-NF-κB; and (MAPKs)-including p38, ERK1/2 and JNK- in PCP-exposed A549 lung- and HepG2 liver cells. Our overall clinical relevance suggests that PCP has the ability to induce an inflammatory response in A549 lung- and HepG2 liver cells and that the collaboration between p/38/MAPK and NF-kB promotes the activation of inflammatory mediators.

Graduate Student Presentations

Fabrication of Human-Scaled Biliary Trees Surgical Replacements through 3D Printing

Ms. Adeola Adedokun-Afolayan, Dr. J. S. Alexander

Louisiana State University Shreveport, LSU Health Sciences Center Shreveport

Fabrication of biliary trees through three-dimensional (3D) printing is a combination of manufacturing methods techniques that has a great potential in a variety of future patient-specific medical technologies. This experiment was able to prove crosslinked polyvinyl alcohol (XL-PVA) 3D printed stent infused with human primary cholangiocytes. The bio-fabrication method in this study was done by fabricating 3D printed stents and infusion of primary cholangiocytes for immediate prototyping of customized living biliary stents with clinical application in the patients with malignant and benign bile duct obstruction. These cholagiocytes infused hepatobiliary (bile duct) stent device created through 3D bioprinting may facilitate suitable placement, provide protective matrix against the bile constituents, potentially limit the development of biofilms in the bile duct and limit infection. In general, this method allows physicians to create personalized bio-integrating stents for use in the biliary procedure and give a new direction for new patient-specific stent fabrication technique.

In-Silico molecular docking reveals novel mechanism of action for YM155, an orphan drug with strong preclinical efficacy in anaplastic thyroid cancer.

Mrs. Aishat Adewoye, Dr. Paul Weinberger

Louisiana State University Shreveport, Louisiana State University Shreveport, Ochsner LSU-Health Shreveport

YM155 is an orphan chemotherapy drug with demonstrated activity as a survivin suppressant, however efficacy in phase II trials was poor and showed no correlation with survivin expression. A recent high-throughput screening study by the NCI surprisingly identified YM155 as having strong efficacy against Anaplastic Thyroid Cancer (ATC) both in-vitro and in-vivo. Based on our previous study showing YM155 inhibited topologic enzymatic function of human topoisomerase II-alpha (hTop2a) in cell-free experiments, we set out to perform molecular docking in-silico to identify potential YM155hTop2a interaction sites. High-resolution crystal structure of human Top2a (1ZXM) complexed with AMPPNP was retrieved from the Protein Data Bank (PDB) database. Using AutoDock Vina 4.2 software, the crystal structure was refined including removal of heteroatoms and water molecules and assignment of Gasteiger charges. We chose as control ligands the known Top2a poison doxorubicin and known top2a catalytic inhibitors Daurinol and Salvicine. Control ligand and YM155 3D geometries were obtained from the PubChem Open Chemistry Database and converted to PDB format in Spartan. Docking was performed in AutoDock Vina including hTop2a dimer, magnesium, water, and each ligand individually, with subsequent visualization using Pymol. As expected, the control ligands Daurinol and Salvicine interacted with Top2a at the ATP binding pocket with -7.2 to -9.8 Kcal/mol binding energies, while doxorubicin had no predicted interaction in that region but did interact at the DNA-binding region with -9.8 Kcal/mol binding energy. Surprisingly, YM155 also strongly interacted with the Top2a ATP-binding pocket with binding energies -8.2 to -8.8 Kcal/mol. Pymol graphics systems allowed delineation of amino acids participating in this interaction via hydrogen bonds and hydrophobic interactions as well as significant interaction with magnesium at the binding site.

Graduate Student Presentations

To determine the role of FOXO transcription factors in regulating cigarette smoke-induced autophagy

Ms. Prathyusha Bagam, Dr. Vladimir Chouljenko

Southern University and A&M College, LSU School of Veterinary Medicine

Cigarette smoking (CS) is the chief etiological factor for Chronic Obstructive Pulmonary Disease (COPD). Oxidative stress induced by CS results in DNA/protein damage, release of reactive oxygen species (ROS) and cell death. In this regard the autophagy mechanism has been shown to play critical role in regulating inflammatory responses, maintaining protein and organelle homeostasis and cellular viability in smoke-related pathologies. Expression and activation of autophagy proteins is regulated by Fork head box class O (FOXO) transcription factors. Our preliminary findings revealed CS-extract (CSE) mediated induction of inflammatory responses and regulation of transcription factors FOXO3a and FOXO1 in human lung adenocarcinoma cells with type II characteristics (A549). We thus hypothesized important role of FOXO transcription factors in CSE-induced inflammation and autophagy. To test our hypothesis, we challenged A549 cells with CSE for 24 hr. Our findings revealed significantly reduced expression of FOXO3a in CSE-exposed A549 cells as compared to control. Contrarily, we observed increase in the expression of FOXO1 in challenged cells. We next studied the effect of CSE-challenge on FOXO3a or FOXO1 knockdown in A549 cells using SiRNA mediated approach. Interestingly, FOXO3a knockdown further augmented CSE-mediated IL-6, CCL-2 and IL-8 production in A549 cells. Moreover, regulation of several autophagy proteins (mTOR, Beclin-1, ATG12, ATG16 ATG5 and LC3A/B) and antioxidant enzymes (MnSOD and catalase) was observed in CSE-challenged FOXO3a knockdown A549 cells. We observed transcriptional induction of FOXO1 in FOXO3a knockdown challenged cells. To further elucidate the role of FOXO1 in CSE-induced autophagy FOXO1 was knocked down. Our results showed reduced expression of autophagy proteins in FOXO1 knockdown cells compared to SiRNA-transfected cells challenged with CSE. Additionally, using ChIP assays we observed increase in the binding of FOXO1 at the promoter regions of autophagy genes- Beclin-1, ATG5, ATG12, ATG16, and LC3B in CSE-challenged A549 cells. Overall, our results provide evidence for FOXO3a-dependent FOXO1-mediated regulation of autophagy in CSE challenged cells. .

GRAPE BERRY EXTRACTS AND ELLAGIC ACID METABOLITES RESCUE PROTEIN HOMEOSTATSIS MECHANISMS: IN VITRO SMOKING/VAPING MODEL

Ms. Rizwana Begum, Dr. Sanjay Batra

Southern University and A&M College

Chronic Obstructive Pulmonary Disorder (COPD) is a progressive and irreversible inflammatory condition which results in severe lung injury. Cigarette smoke (CS) exposure, either first or second hand, accounts for more than 90% of reported cases. Understanding the molecular mechanisms associated with the pathogenesis of COPD is limited, partly because of the complex nature of the disease.Muscadine grape berry extract (MGBEs)are rich in secondary metabolites (SMs) like flavonoids and stilbenoids which are known to possess antioxidant, anti-cancer, anti-inflammatory, antimicrobial properties. We tested the effects of MGBE on CS-extract (CSE) induced responses in terms of inducible proteasome subunits and autophagy related proteins. The recent outbreak of vaping-related deaths across the US has sparked extensive debate related to the use of e-cigarettes as safer alternatives to conventional smoking. Our results show significant increase in the production of cytokines/chemokines and noticeable increase in

the expression of LMP2 (iβ1) and MECL1 (iβ2), the inducible proteasome subunits in TF-ECVC (1%)-challenged A549 cells.Our findings provide the preliminary evidence about the possible dysregulated proteasome/immunoproteasome function in TF-ECVC challenged cells. Ellagic acid metabolites (EAM) have been studied extensively as anti-cancer and anti-inflammatory agents in various study models. We therefore explored if EAM,Urolithin A (Uro-A) and Urolithin C (Uro-C) can combat with dysregulated protein homeostasis mechanisms and inflammation caused by TF-ECVC in A549 cells. Interestingly, both Uro-A and Uro-C were able to rescue A549 cells from TF-ECVC induced responses in terms of cytokines/chemokines production and the expression of inducible proteasome subunits. Overall, our results demonstrate that MGBEs and EAM possess significant potential to mitigating smoking/vaping induced inflammation and dysregulated protein homeostasis mechanisms.

Fusarochromanone as a Therapeutic for Prostate Cancer

Mr. Nafay Hayat, Dr. Xiuping Yu

Louisiana State University Shreveport, LSU Health Science Center Shreveport

Prostrate cancer has remained a significant human health problem in a majority of western countries. In the United States, it is the most common non-skin cancer and second leading cause of cancer related deaths in men. Androgen deprivation therapy has proven useful in the treatment of advanced prostate cancer (PCa). However, overtime the tumors become resistant to androgen deprivation and almost always progress to castration-resistant PCa (CRPC). Activation of the Wnt/β-Catenin signaling pathway and upregulation of androgen receptors have been implicated in the progression of PCa to CRPC. Additionally, dysfunction in the autophagy cell cycle in cells is associated with PCa progression and survival. Fusarochromanone (FC101) is a small flavonoid molecule shown to have anti-cancer effects in several types of cancer. The goal of this project is to observe the effect of FC101 in PCa. Primary epithelial cells derived from normal human prostate tissue and cancerous prostatic cell lines were treated with various concentration of FC101. Cell proliferation assays and luciferase assays were performed. Results showed that FC101 displays potent anti-proliferation activity in PCa. Specifically, FC101 treatment of PCa cells induces G1 phase cell cycle arrest. Additionally, it was found that FC101 treatment suppressed the activity of Wnt/beta-Catenin signaling in PCa cells thus resulting in reduced PCa proliferation. Finally, PCa cells treated with FC101 resulted in down-regulation of autophagic biomarkers. This was in comparison to PCa cells treated with chloroquine as a control. From our results we conclude that FC101 causes cell cycle arrest, decreased cell proliferation, and down-regulation of autophagic biomarkers in PCa.

Phylogenetic Posterior Predictive Assessment on a Fossilized Birth-Death Model

Ms. Christina Kolbmann, Dr. Jeremy Brown

Southeastern Louisiana University, Louisiana State University

Formicidae species are a model group for studying diversification, because of their extensive collection records, geographic range, social complexity, and pathogen-like evolution. Large molecular, morphological, and fossil age datasets were integrated in a Fossilized BirthDeath (FBD) analysis to test the flexibility of the Phylogenetic Posterior Predictive assessment (P3) to determine the fit of diversification models and time-stratified datasets. Functions from the R package FossilSim and TreeSim were used to mimic the P3 process for FBD models. A RevBayes tutorial 'Introduction to Posterior Prediction' was also created for introductory comprehension and non-phylogenetic analysis.

Design, synthesis, and evaluation of grafted peptides/peptidomimetics for the inhibition of protein-protein interactions of EGFRs in osteosarcoma

Mr. Sitanshu Singh, Dr. Sita Withers

University of Louisiana at Monroe, LSU School of Veterinary Medicine

The objective of this project is to understand the role of homo and heterodimerization of epidermal growth factor receptors (EGFRs) in osteosarcoma (OSA) and to design stable peptide-like molecules which will inhibit this protein-protein interaction. In this project, we proposed to inhibit the protein-protein interactions using novel grafted cyclic peptides by targeting EGFR proteins in OSA. Based on our previous studies, we have confirmed that the small cyclic peptides that were grafted with a peptidomimetic, inhibit the interactions of EGFR with HER2 and HER3 in human non-small cell lung cancer (NSCLC) both in in-vitro and in-vivo models. OSA is known to express EGFR-family proteins. Hence, we extended our studies to OSA cell lines that express EGFR proteins. Therefore, our proposed aim was to understand the role of homo and heterodimerization of extracellular domains of epidermal growth factor receptors (EGFRs) in OSA and its inhibition by grafted peptides. We designed, synthesized grafted cyclic peptides and evaluated the cell viability in OSA cells that express EGFR-family proteins. Further, we evaluated the EGFR/HER2/HER3 protein expressions and assessed the molecular mechanism of inhibition of protein-protein interaction in human and canine OSA. To understand the immunogenicity of the peptides, a splenocyte proliferation assay was performed in an animal model, which suggests that our peptide was non-immunogenic in animals. These preliminary studies indicated that the grafted cyclic peptide showing promising results to inhibit the dimerization of EGFRs in OSA, hence they can have the potential to be developed further into therapeutic agents.

Expression levels of Mediator kinase module subunits and their interaction with transcription factors in mouse adipose tissue

Ms. Sree Venigalla, Dr. Jackie Stephens

Louisiana Tech University, Pennington Biomedical Research Center

Obesity is currently a major epidemic with obesity-related metabolic disorders such as type 2 diabetes, liver disease, and heart disease becoming more common. Dysregulation of genes associated with glucose and/or lipid metabolism is common in obesity-related disorders. Understanding how transcription factors and their cofactors regulate glucose/lipid metabolism has been a focus of many studies. Mediator is a large evolutionarily conserved transcriptional coactivator that directly binds to gene-specific transcription factors and RNA Pol II. The kinase domain, a dissociable four subunit module of the Mediator complex is made of subunits MED13, MED12, CDK8, and CCNC, that controls the expression of different subsets of genes to direct cell fate1. Recent studies have shown that the kinase module is dissociated and degraded under feeding-induced activation of nutrient signaling in mouse livers2,3. However, the downregulation of kinase module proteins in adipose tissue was not examined. This study determines the expression of protein levels of the kinase module subunits between fasting and feeding in mouse adipose tissue depots where the expression of kinase subunits appears to remain constant in all adipose tissues when

mice are fasted. However, following feeding the protein levels of subunits of the kinase module are decreased in most white adipose tissues except for mesenteric white adipose tissue (mWAT) and brown adipose tissue (BAT). Immunoprecipitation data provides evidence that MED12 and CDK8 interact differentially with transcription factors including STAT5A, CREBPa, PPARg, and SREBP-1c in preadipocytes and mature adipocytes. Future work will identify molecular details concerning the mechanism through which Mediator is involved in the regulation of metabolism under physiological and pathophysiological conditions. Understanding these molecular mechanisms aids in identifying novel therapeutic targets for the treatment of metabolic disorders.

Poster Session Abstracts

Poster Session Abstracts

1 **Targeting PCSK9 secretion and interaction with LDL receptor as a novel strategy to suppress the hormone dependent breast cancer recurrence**

Mr. Khaldoun Abdelwahed, Abu Bakar Siddique, Mohamed Mohyeldin, Mohammed Qusa, Sitanshu Singh, Amira Goda, Seetharama Jois, Khalid El Sayed
University of Louisiana at Monroe

Hypercholesterolemia has been documented to drive hormone-dependent breast cancer (BC) progression and resistance to hormonal therapy. Proprotein convertase subtilisin/kexin type-9 (PCSK9) regulates cholesterol metabolism through binding to LDL receptor (LDLR) and targeting the receptor for lysosomal degradation. Inhibition of PCSK9 is an established strategy to treat statins non-responsive hypercholesterolemia. Pseurotin A (PS) is a unique spiro-heterocyclic γ-lactam alkaloid isolated from the fungus Aspergillus fumigatus. Preliminary studies indicated that PS lowered PCSK9 secretion in cultured HepG2 hepatocellular carcinoma cells, with an IC50 value of 1.20 µM. Docking studies suggested the ability of PS to bind at the PCSK9 narrow interface pocket that accommodates LDLR. Surface plasmon resonance (SPR) showed PS ability to inhibit the PCSK9-LDLR interaction at a concentration range of 10-150 µM. PS showed an in vitro dose dependent reduction of PCSK9 level, along with an increased LDLR levels in hormone-dependent BT-474 and T47D BC cell lines. In vivo, PS suppressed the progression of BT-474 BC cells in orthotropic nude mouse xenograft model. PS also effectively suppressed locoregional recurrence of BT-474 BC cells after primary tumor surgical excision. Western blot analysis showed decreased PCSK9 expression in liver tissues of treated mice compared to control. PS treatment significantly reduced PCSK9 expression and normalized LDLR level in collected primary and recurrent tumors at the study end. PS-treated mice showed reduced plasma cholesterol and 17β-estradiol levels. Inhibition of tumor recurrence was associated with significant reductions in plasma level of the human BC recurrence marker CA 15-3 in PS-treated mice. The results of this study provide the first evidence of PS as a novel first-in-class dual PCSK9 secretion and protein-protein interaction inhibitor for the suppression of the hormone-dependent BC tumor progression and recurrence.

2 **Fabrication of Human-Scaled Biliary Trees Surgical Replacements through 3D Printing**

Dr. Adeola Adedokun-Afolayan, J.S.Alexander, C.J Boyer, Hrishikeh Samant, A. Wayne Orr, Mabruka Alfaedi, U. Cvek
Louisiana State University Shreveport, LSUHSC-Shreveport

Fabrication of biliary trees through three-dimensional (3D) printing is a combination of manufacturing methods techniques that has a great potential in a variety of future patient-specific medical technologies. This experiment was able to prove crosslinked polyvinyl alcohol (XL-PVA) 3D printed stent infused with human primary cholangiocytes. The bio-fabrication method in this study was done by fabricating 3D printed stents and infusion of primary cholangiocytes for immediate prototyping of customized living biliary stents with clinical application in the patients with malignant and benign bile duct obstruction. These

cholagiocytes infused hepatobiliary (bile duct) stent device created through 3D bioprinting may facilitate suitable placement, provide protective matrix against the bile constituents, potentially limit the development of biofilms in the bile duct and limit infection. In general, this method allows physicians to create personalized bio-integrating stents for use in the biliary procedure and give a new direction for new patient-specific stent fabrication technique.

3 **In-Silico molecular docking reveals novel mechanism of action for YM155, an orphan drug with strong preclinical efficacy in anaplastic thyroid cancer.**

Mrs. Aishat Adewoye, Qinqin Xu, Ryan MacCay, Prerana Ramesh, Chris Stratton, Paul Weinberger, Dr. Mahdavian.

Louisiana State University Shreveport, Ochsner LSU-Health Shreveport

YM155 is an orphan chemotherapy drug with demonstrated activity as a survivin suppressant, however efficacy in phase II trials was poor and showed no correlation with survivin expression. A recent high-throughput screening study by the NCI surprisingly identified YM155 as having strong efficacy against Anaplastic Thyroid Cancer (ATC) both in-vitro and in-vivo. Based on our previous study showing YM155 inhibited topologic enzymatic function of human topoisomerase II-alpha (hTop2a) in cell-free experiments, we set out to perform molecular docking in-silico to identify potential YM155hTop2a interaction sites. High-resolution crystal structure of human Top2a (1ZXM) complexed with AMPPNP was retrieved from the Protein Data Bank (PDB) database. Using AutoDock Vina 4.2 software, the crystal structure was refined including removal of heteroatoms and water molecules and assignment of Gasteiger charges. We chose as control ligands the known Top2a poison doxorubicin and known top2a catalytic inhibitors Daurinol and Salvicine. Control ligand and YM155 3D geometries were obtained from the PubChem Open Chemistry Database and converted to PDB format in Spartan. Docking was performed in AutoDock Vina including hTop2a dimer, magnesium, water, and each ligand individually, with subsequent visualization using Pymol. As expected, the control ligands Daurinol and Salvicine interacted with Top2a at the ATP binding pocket with -7.2 to -9.8 Kcal/mol binding energies, while doxorubicin had no predicted interaction in that region but did interact at the DNA-binding region with -9.8 Kcal/mol binding energy. Surprisingly, YM155 also strongly interacted with the Top2a ATP-binding pocket with binding energies -8.2 to -8.8 Kcal/mol. Pymol graphics systems allowed delineation of amino acids participating in this interaction via hydrogen bonds and hydrophobic interactions as well as significant interaction with magnesium at the binding site.

4 **Unfolded protein response regulates P53 expression in pulmonary endothelium.**

Mr. Mohammad Shohel Akhter, Mohammad Afaz Uddin, Nektarios Barabutis

University of Louisiana at Monroe

The pulmonary endothelium is a continuous monolayer which regulates the transfer of

macromolecules, nutrients, leucocytes and blood fluid across the vascular wall. Dysfunction of this endothelial barrier causes pulmonary hyperpermeability, which eventually may lead to Acute Respiratory Distress Syndrome (ARDS). Both the Unfolded Protein Response (UPR) and P53 have been previously shown to exert anti-inflammatory activities in human tissues. In this study, we investigated the role of UPR modulation in the pulmonary P53 expression. We employed a variety of UPR activators and inhibitors to regulate UPR activation in bovine lung cells, and we consequently measured the expression levels of P53. Bovine Pulmonary Arterial Endothelial Cells (BPAECs) treated with the UPR inductors brefeldin A (2µg/ml), dithiothreitol (1mM) and thapsigargin (1µM); increased P53 expression levels compared to the vehicle-treated cells. On the other hand, the UPR inhibitors N-acetyl cysteine (1mM), kifunensine (5µM), and ATP-competitive IRE1α kinase-inhibiting RNase attenuator (1µM) suppressed the levels of this Guardian of the Genome compared to the vehicle-treated cells. The present study demonstrates the positive regulation of P53 by UPR, and future endeavors will reveal the exact mechanisms mediating those effects. The present study was supported by the R&D, Research Competitiveness Subprogram (RCS) of the Louisiana Board of Regents through the Board of Regents Support Fund (LEQSF(2019-22)-RD-A-26) and the National Institute of General Medical Sciences of the National Institute of Health (5P20GM103424-15, 3P20GM103424-15S1).

5 Characterization of Streptomyces sp. COUK1 and evaluation of its antimicrobial potential

Mr. Olaitan Akintunde, Bert Lampson
University of Louisiana Lafayette, East Tennessee State University

Streptomyces are known to produce a wide range of antibiotics and other bioactive compounds with remarkable industrial importance. Streptomyces sp. COUK1 was discovered as a contaminant on a plate in which Rhodococcus erythropolis was used as a test strain in a disk diffusion assay and produced a zone of inhibition against the cultured R. erythropolis. The identity of the contaminant was confirmed as Streptomyces through 16S rRNA sequencing as well as phenotypic and biochemical properties. This Streptomyces produces a strong inhibitory compound in different growth media. A culture extract from inorganic salts starch agar was found to be very active; producing a large zone of inhibition against several Gram-positive and Gram-negative test strains. The active molecules in this extract have been detected via chromatographic analysis and disk diffusion assay. The difference in the antibacterial activity and chromatographic properties of extracts recovered from different growth media suggests that this Streptomyces strain could produce more than one type of inhibitory compound.

6 Inhibition of FXIIIa by Sulfonated Molecules as Potential Avenue to Novel Anticoagulants

Dr. Rami Al-Horani, Srabani Kar, Madhusoodanan Mottamal
Xavier University of Louisiana

Purpose. Thrombosis remains a major public health crisis. Current treatment entails the use

of anticoagulants which, despite their efficacy, are associated with significant bleeding. Thus, new approaches to safely treat thrombosis are needed. Factor XIIIa (FXIIIa) is a transglutaminase that catalyzes the last step in the coagulation process. Interestingly, venous thrombi from FXIII-deficient mice were significantly small. Studies also revealed that specific FXIIIa polymorphism protects against venous thrombosis and that heterozygous FXIII-deficient mice do not suffer from excessive bleeding. Thus, FXIIIa has been targeted to develop new anticoagulants with minimal bleeding. Few orthosteric FXIIIa inhibitors were reported, yet none was selective. We have proposed to develop allosteric inhibitors so as to achieve selectivity. Methods. A library of sulfonated molecules was screened for FXIIIa inhibition in a transglutamination assay. The effect on fibrin polymerization as well as the inhibition mechanism and selectivity were evaluated. Cellular toxicity was assessed using a proliferation assay. Molecular modeling was exploited to determine the inhibitors' putative binding site. Results. Four molecules inhibited FXIIIa with IC50 of <5 µM. The inhibitors also affected fibrin polymerization. Michaelis-Menten kinetics revealed a mixed mechanism of inhibition. The best inhibitor was >200-fold selective over thrombin and factor Xa and 8-fold selective over tissue transglutaminase-2. It doubled the clotting times of human plasma but only at concentrations >700 µM. It did not affect the proliferation of three cell lines at 10 µM. Molecular modeling indicated that inhibition of FXIIIa may stem from binding to an anion-binding site involving K73, R68, K61, R56, & K54. Conclusion. The study reports two potent and potentially nonactive site inhibitors of FXIIIa belonging to two chemotypes. The inhibitors will be used in future efforts to develop effective and safer anticoagulants.

7 **Apoptosis and Cell cycle arrest induced by anticancer drug cabazitaxel in prostate cancer cells**

Mr. Ira Baggett, Sugandhi Muthyala, Desirae George-McCool , Eduardo Martinez-Ceballos ,Konstantin Kousoulas, Xiaoping Yi
Southern University and A&M College, LSU School of Veterinary Medicine

Prostate cancer is the most common cancer among American men. Although new treatments for prostate cancer continue to be investigated, no definitive cure has been found for the advanced aggressive stages. The anticancer drug Cabazitaxel is a semi-synthetic, toxoid derivative used for the treatment of hormone-refractory prostate cancer. The molecular basis of this drug needs to be extensively studied using a cell culture model that best emulates the tumor environment in the body. We hypothesized that Cabazitaxel may be effective in inducing apoptosis by inhibiting or acting on some signaling pathways in cultures of prostate cancer cells. In this research, we investigated the effect of Cabazitaxel on cell cycle arrest and apoptosis in cultures of prostate cancer cells. The DU-145 cell line was treated with different dosages of Cabazitaxel and evaluated by apoptosis and cell cycle progress. Our results indicated that Cabazitaxel has an effect of decreasing cell viability from 80% of untreated cells to about 30% of those treated with cabazitaxel 10 nM and induced apoptosis after three days. The Cabazitaxel also blocked the transition of cells in the G0/G1 to S phase, but less effectively in G2/M phase. The current study demonstrates that Cabazitaxel treatment may induce cell cycle arrest by modulating key regulators. Further investigation for

the molecular mechanism of Cabazitaxel action in prostate cancer cells is still in progress.

8 The Anticoagulant Properties of Lignosulfonic Acid Sodium

Ms. Page Bankston, Srabani Kar, Rami A. Al-Horani
Xavier University of Louisiana

Purpose: Heparins are mixtures of sulfated polysaccharides that have been used as anticoagulants for >90 years. Heparins promote such activity via activating antithrombin, a serpin that inhibits thrombin and factor Xa. Importantly, 60% of the US supply of porcine heparins is imported from China. In 2008, at least 81 deaths and 785 injuries were linked to contaminated heparins. Currently, there is a serious concern over the heparin supply because of the deadly African swine fever outbreak which has affected China since August 2018 and has led to the death of ~2 million pigs. Thus, alternatives to heparins are in urgent need. In this study, we investigated the anticoagulant activity of lignosulfonic acid sodium (LSAS), a nonsaccharide heparin mimetic. LSAS is a relatively safe industrial byproduct with similar polyanionic characteristic to that of heparin. Methods & Results: Human plasma clotting assays, fibrin polymerization testing, and enzyme inhibition assays were exploited to investigate the anticoagulant activity of LSAS. In normal plasma, LSAS doubled APTT at ~262 µg/mL, yet it did not double PT or TT at the highest concentration of 363 µg/mL. Likewise, LSAS doubled APTT at ~271 µg/mL in antithrombin-deficient plasma. Yet, LSAS doubled APTT at higher concentrations of 609 and 370 µg/mL using heparin cofactor II-deficient and factor XI-deficient plasmas, respectively. LSAS did not affect FXIIIa-mediated fibrin polymerization at 1000 µg/mL. Enzyme assays indicated that LSAS inhibits factor XIa with IC50 value of ~8 µg/mL. LSAS did not inhibit thrombin, factor Xa, or factor XIIIa at the highest concentrations tested. Conclusion: LSAS is a sulfonated heparin mimetic that demonstrates a significant anticoagulant activity in human plasma. Mechanistically, it appears to be potent and selective inhibitor of factor XIa and perhaps heparin cofactor II activator. Overall, this study introduces LSAS as a promising lead for further development as an anticoagulant.

9 Kinetic Analysis of the Impact of LDH on Cancer and HGPRT Inhibition for Malaria

Dr. Daniel Barnes, Razan Qamar, Zoe McKean, Daniel Barnes
Southeastern Louisiana University

This project's goal is to generate stable expression hosts for enzymes associated with malarial vectors and aerobic glycolysis in cancerous cells. The expression and isolation of these enzymes via recombinant E. coli will allow for their kinetic characterization in the presence and absence of potential small molecule inhibitors that may serve as an avenue for drug development. A vector expressing Plasmodium HGXPRT has been acquired, and the enzyme has been successfully expressed and extracted. The current activity assay for HGXPRT relies on the UV absorption characteristics of guanosine monophosphate at 257nm. This is problematic due to several molecules with similar absorption characteristics providing background absorbances. Therefore a coupled assay using IMPDH and detecting the production of NADH at 340nm is being studied. An E. coli vector expressing human IMPDH

has been acquired and the enzyme has been successfully expressed and assayed. A coupled assay using both enzymes is currently being optimized. It is hoped that this system can be used to test potential inhibitors on HGXPRT for the development of antimalarial drugs targeting the purine salvage pathway. Additionally, an expression vector for human LDH5 is being developed. This vector will allow for ready expression and mutation of LDH5 in order to describe the impacts of the enzyme in the development and sustainment of aerobic glycolysis in cancerous cells, also referred to as the Warburg effect. The in-house production of this enzyme will allow for the study of the wild-type versus known and putative mutations of the enzyme as well as the potential development of small molecule inhibitors in order to target cells undergoing aerobic glycolysis. The core of this research is the understanding of the molecular mechanisms underlying disease, and this project focuses on the integration of undergraduate student researchers at every level of project planning and implementation.

10 **Tunable Biomimetic Scaffolds for Directing Stem Cell Growth and Differentiation for Tissue Regeneration Applications**

Mrs. Haley Barnett, India Pursell, Rachel Hegab, Nellie Perez, Jamie Newman, Mary Caldorera-Moore
Louisiana Tech University

The effect of prolonged exposure to microgravity, space radiation, extreme temperature cycling, and exposure to ultra-vacuum and atomic oxygen conditions on skeletal muscle during spaceflight is not well understood. The neuromuscular system is thought to be the bodily system most affected by microgravity environments causing rapid muscle degeneration, reduced function, and skeletal muscle fatigue. My project aims to create a functional skeletal muscle patch that can be used to study the effects of spaceflight on skeletal muscle degeneration in vitro. Previously, our lab has developed a tailorable poly(ethylene glycol) dimethacrylate (PEGDMA) hydrogel scaffold in which human adipose-derived stem cells have been successfully seeded and remained viable. The challenge in producing a skeletal muscle scaffold lies in reproducibly differentiating stem cells on these materials to desired lineages. Despite the volume of research being conducted in this area, the interactions between stem cells and the external environment of biomaterial substrates are not well understood. My research will investigate how extracellular cues, specifically elasticity and surface chemistry of a biomaterial influence stem cell fate. This will be accomplished by synthesizing PEGDMA hydrogels of varying elasticities and surface functionalizing them with the protein collagen type I. This research will lead to a better understanding of how stem cell environment determines cell fate and then be used to consistently direct differentiation towards a myogenic lineage. This will lead to the design of an innovative and adaptable hydrogel biomaterial to investigate the effect of spaceflight on skeletal muscle tissue.

11 **Potent anti-proliferative and pro-apoptotic effects of Celastrol encapsulated in poly(ε-caprolactone) nanoparticles both human melanoma and non-melanoma growth in vitro**

Mr. Samuel Boateng, Tithi Roy, Roxane-Cherille Chamcheu, Sergette Banang-

Mbeumi, Vanna Sanna, Jean Christopher Chamcheu
University of Louisiana at Monroe, University of Sassari, Italy

The quest to salvage the predicaments from the two main forms of cutaneous cancers; melanoma (MSC) and non-melanoma (NMSC) skin cancers, is a pressing wake-up call considering the worldwide increasing incidence over the years, especially in the United State (US). NMSC which encompasses basal cell carcinoma (BCC), and squamous cell carcinoma (SCC) is estimated to affect an alarming 3 million people in US yearly, and this excludes the more aggressive and fatal MSC reported. Many therapies tailored against these carcinomas have been confounded with resistances and adverse effects. Celastrol a natural occurring phytochemical triterpenoid from the root of tripterygium wilfordii, exert a multifaceted arsenal of activity; anti-oxidant, and anti-inflammatory effect, which are desirous against drug resistance and adverse reactions associated with chemotherapy. In spite of these therapeutic effects, some physicochemical and pharmacological properties such as solubility, bioavailability and systemic toxicity restricted its usage. This study employed celastrol alongside developed a biocompartible polymeric poly(ε-caprolactone) nanoparticles (NPs) encapsulating celastrol (CL) which significantly decreases the limitation related with the unformulated celastrol. In this study, the effects of CL and nano-CL was investigated on proliferation, motility, wound closure and clonogenic potential in three forms of human cell lines; MSC (A375), NMSC (A431) and (normal cells) HaCaT. CL and nano-CL treatment (0.01-5µM) resulted in a significant dose and time-dependent decrease in cell growth, viability, wound closure, colony formation and cell cycle with minimal effect on normal cells. Interestingly, the proof-of-principle shows that nano-CL exhibits greater than ten-fold dose advantage over non-encapsulated CL in human MSC (A375) and NMSC (A431) cells in vitro. Translation of these data to appropriate animal model systems could pave way for safer and effective management of skin cancer.

12 The Role of Notch Signaling in Adult Stem Cell Self-Renewal and Myogenic Differentiation

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Human Adipose Derived Stem Cells (hASCs) have significant therapeutic potential due to their ability to self-renew, differentiate, and modulate the immune system. In order to harness the therapeutic power of these cells we must first understand how cell state and differentiation are regulated. The Notch Signaling Pathway is a highly conserved signaling cascade involved in various aspects of organismal development and has been shown to regulate the multipotent differentiation of hASCs. By studying the mechanisms of the Notch Pathway in self-renewing cells, we can begin to piece together how this pathway regulates and determines cell fate. Once this mechanism is understood, it can be manipulated by targeting certain components of the pathway to lead to a desired form of differentiation. The ability to selectively differentiate these cells into muscle tissue (myogenesis) holds significant clinical

relevance. If this process were to be fully optimized, it could lead to autologous transplants of muscle cells grown from hASCs harvested from the patient's own adipose tissue. Investigating the role that the Notch Pathway plays in myogenesis could lead to targeted manipulation of this pathway to increase myogenic potential.

13 **Topical application of fisetin alleviates psoriasis-like disease via inhibiting mTOR-mediated signaling pathways in Balb/c mice**

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Treatment for moderate to severe psoriasis remains elusive. Dysregulation of the central mTOR signaling has emerged as a clinically relevant target for psoriasis. Hence, developing agents that inhibit their activities could potentially be beneficial for psoriasis management. We earlier reported that fisetin, a dietary 3',4',7 trihydroxyflavonol, is a potent mTOR kinase inhibitor (Biochem Pharmacol.;89(3):349-60.), and recently showed how it attenuates psoriasis-like features in vitro (Cells. 2019 Sep 15;8(9). pii: E1089.). Here, we examined the effect of fisetin in-vivo using an imiquimod (IMQ)-induced psoriasiform disease model in Balb/c mice, and begun generating a myeloid lineage mTOR knockout mouse model for validating the concept. Topical application of IMQ cream induced mouse psoriasis-like skin lesions characterized by increased erythema, ear swelling (acanthosis and hyperkeratosis), and scaling; immunohistopathological analysis revealed the activation of Akt/mTOR pathway when compared to matched control tissues. Lesional skin tissue sections of mice topically treated with fisetin (1mg/cm2 of shaved skin/ear, daily) exhibited significant decrease in i) psoriasiform hyperplasia including ear swelling and epidermal thicknesses, ii) erythema, iii) levels of inflammatory mediator and cytokines (IL-22 and iNOS) and iii) proliferation (Ki-67) when compared with control mice. Furthermore, fisetin-treated lesional skin tissue sections showed decrease in the phosphorylated forms of Akt and mTOR and downstream targets. In view of confirming the role of mTOR in this disease, we have started generating myeloid lineage mTOR knockout mice to be used in valuating the role of myeloid-lineage mTOR in the pathogenesis of psoriasis. Collectively, our data affirm mTOR involvement in psoriasis and suggest fisetin as a modulator alone or as an adjuvant to current therapies. Validating these in the myeloid lineage mTOR deficient mice will provide translational data that could be useful for treating psoriasis and potentially other hyperproliferative skin diseases.

14 **Understanding the Role of Conformational Changes in Kinesin-5**

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Xavier University of Louisiana

In processive kinesins, motor domains proceed forward in a hand-over-hand stepping

fashion, while performing ATP hydrolysis. Several of these biological nanomotors have been identified as very promising targets for potential cancer therapy such as Kinesin-5 and Kinesin-6. However, the overall mechanism of inhibition in these targets needs further exploration. Inspection of the crystal structures of kinesin dimers reveals the addition of strands to the central beta-sheet is found in one head and absent in the other; this previously unrecognized structural asymmetry between the two heads may suggest a regulatory mechanism. What has been ignored is that the docking of the NL and cover-neck to the motorhead coordinates two-strand additions to the central beta-sheet. During docking the NL forms two beta-strands, (Beta (9) and Beta (10), form a sheet with Beta (0) of the cover-neck and (Beta7 of the central Beta-sheet, respectively. These structural changes in the neck-linker and cover-neck of Kinesin-5 have not been reported as there is currently no dimeric structure for this protein. Thus, the importance of establishing this conformational switch in Kinesin-5 requires additional experiments for understanding and molecular validation. Will the length of the neck-linker interfere with the coordination? To study this, we have generated inserts of three residues (DAL) into strategic positions along the neck-linker of the dimeric Kinesin-5 construct (Eg5-513). We have expressed these mutants and are pursuing purification in a bacterial system. We expect a loss of interaction between Beta (7) and Beta (0). We anticipate that this will lead to total loss of kinesin stability. This work would provide a crucial link to understanding the complete mechanism of inhibition in these targets for future therapeutic benefit.

15 **Mobile app to improve detection of undiagnosed diabetes and pre-diabetes**

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Diabetes mellitus is a class of metabolic dysregulation characterized by hyperglycemia, a prolonged elevation in blood sugar. In addition to Type 1 diabetes (caused by a loss of beta cells in the pancreas), it frequently manifests itself as Type 2 diabetes (insulin resistance) and gestational diabetes (diabetes during pregnancy). It is estimated that 425 million people worldwide (or 8.8% of the adult population) has some form of diabetes, with about 90% of cases corresponding to Type 2 diabetes. In 2015 alone, an estimated 30.3 million Americans (9.5% of the population) had some form of diabetes, and an estimated 7.2 million cases remained undiagnosed. More worryingly, 84.1 million Americans had pre-diabetes, a known risk factor for Type 2 diabetes. We developed a pre-screening utility for the iOS and Android platforms to provide guidance to patients who believe they may be at risk for diabetes. This application provides users a brief nine-item questionnaire involving questions concerning age, body measurements, and diabetes-related medical history. This data is then fed into a decision tree classifier to predict the user's diabetes risk category and deliver a recommendation to the user. A usability study was then performed on a random sample of students (n=20) using the Android and iOS implementations of our application. We provided a survey of nine Likert-scale items and two free form questions designed to obtain the users' perceptions of the software. Additionally, vocal responses by user (including questions about

usage) were recorded. This study was developed in collaboration with Feist-Weiller Cancer Center's (FWCC) Partners in Wellness mobile screening units that provide free screenings to financially qualified uninsured or under-insured individuals across half of Louisiana as far as Bunkie, Oakdale and Kinder.

16 Conformationally Constrained Multicyclic Grafted Peptide as an Immunomodulator

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University of Louisiana at Monroe

Immune system mechanism can be regarded as double edge sword; one edge is for protecting our body against foreign antigens and eliminating them whereas the other edge on activation has detrimental effect leading to self-destruction of our tissues and cells which is referred as Auto-immune disease.CD58 is a co-stimulatory molecule found to be over-expressed in antigen presenting cells(APC) in autoimmune disease like rheumatoid arthritis. Inhibition of CD2-CD58 protein-protein interaction (PPI) that occurs between T-cells and APC can be a potential therapeutic intervention in treatment of such autoimmune disease. From our previous studies by alanine scanning followed by grafting on Sun flower Trypsin Inhibitor (SFTI) we obtained a potent CD2-CD58 PPI inhibitor peptide (SFTI-AS1) with multiple conformations having an IC50 of 37 nM in lymphocyte epithelial cell adhesion assay. In this study our objective is focused on conformational constraining and locking of SFTI-AS1 into a major bioactive conformer peptide. The designed peptide SFTI-DBF has been found to be conformationally locked into major single conformer that is confirmed by NMR studies and molecular dynamics study. SFTI-DBF inhibited adhesion between T-cells and RA cells with an IC50 of 3 nM. Binding study of SFTI-DBF with CD58 is confirmed further by molecular docking, flow cytometry and surface plasmon resonance. Circular dichroism study showed the conformational stability of SFTI-DBF even at higher temperature. Serum stability study, pH stability study and trypsin stability study showed that SFTI-DBF is stable. Also, SFTI-DBF was able to inhibit the activation of T-Cell by Calcium Flux study and was able to inhibit CD2-CD58 PPI evident by Proximity Ligation Assay (PLA). To summarize the study, we have designed a conformationally constrained, stable multicyclic grafted peptide that can inhibit the CD2-CD58 interaction and can be developed as therapeutic immunomodulating agent.

17 Anticancer Activities from Camptothecin-Related Iridoids from Medicinal Plant Camptotheca acuminata

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Camptothecin has been well known as an important chemotherapeutic agent to treat colorectal, ovarian, cervical and lung cancers by inhibiting DNA topoisomerase I. This compound has been solely purified from medicinal plant Camptotheca acuminata with low yields. Camptothecin, like other monoterpene indole alkaloids (MIAs) is derived from precursor iridoids and tryptamine after decarboxylation of tryptophan. In order to investigate camptothecin biosynthetic processes in C. acuminata plants, a transgenic line has been developed by RNA interference (RNAi) silencing of an important tryptophan decarboxylase (TDC) which contributes to the indole moiety of MIAs, Comparative metabolite profiling of this TDC-RNAi line and non-transgenic line has shown that while there is no camptothecin observed, iridoids were significantly increased in the transgenic line. Interestingly, when MDA-MB-231 triple-negative breast cancer cell line was treated with TDC-RNAi line extract, inhibition of cell proliferation was observed. In this study, we compare the cytotoxicity of camptothecin-related iridoids from C. acuminata and camptothecin as anticancer agents. While purification of these potential cytotoxic iridoids from C. acuminata plants has been underway, this study demonstrates the prospect of anticancer drug discovery by alteration of metabolic pathways in medicinal plants.

18 The Autophagy Mechanism: A Friendly Response in Human Airway A549 Lung Cells and TIB-73 Mouse Liver Cells Exposed to Pentachlorophenol

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Grambling State University

Autophagy is a natural and regulated mechanism that removes cellular trash with the help of specific gene proteins. This intracellular clearance is a friend to mammalian cells because it maintains cellular homeostasis and promotes the manufacturing of energy from old lipid and protein molecules. In this study, we are trying to understand the autophagy molecular mechanisms because they are associated with the progression of cancer. Pentachlorophenol (PCP) is an organochlorine fungicide, which has been used as a prevalent wood preservative in the United States (U.S.) for more than 130 years. PCP has a high lipophilicity index and has been established as a human Group B2 carcinogen by the U.S. Environmental Protection Agency using animal model studies. PCP is a persistent environmental pollutant, therefore, our interest is drawn to PCP for its ability to induce systemic toxicity and carcinogenesis. Previous findings from our laboratory have demonstrated that PCP has the ability to induce inflammatory responses in human airway A549 lung cells and TIB-73 mouse liver cells. In this study, we hypothesized that PCP will cause an autophagy response in human airway A549 lung cells and TIB-73 mouse liver cells. Interestingly, we observed increased levels of Beclin-1 (regulator of autophagy), and ATG16 (essential for autophagosome formation), Nrf2 (transcription factor responsible for restoring redox homeostasis), in PCP-exposed A549 cells in a concentration-dependent manner. An accumulation of LCB3, an autophagy marker, also confirmed the autophagy response in the PCP-treated human airway lung cells. In TIB-73 mouse liver cells, we observed an increase in p62/SQSTM1, indicating an autogphagic influx as well as a decrease in LCB3. Overall, these findings provide evidence of autophagy responses in PCP-treated human airway A549 lung cells and TIB-73 mouse liver cells.

19 **Strontium-Coated Clay Nanoparticles for Bone Regeneration**

Ms. Anusha Elumalai, Anusha Elumalai, Yangyang Luo, Ahmed Humayun, and David K. Mills
Louisiana Tech University

The use of strontium (Sr) for bone tissue regeneration has gained in research interest over the past few years due to its beneficial properties in treating bone loss associated with osteoporosis. Osteoporosis increases the chance of bone fracture by decreasing bone mass and increasing its fragility. Since Sr and calcium share many chemical similarities, incorporating Sr nanoparticles in bone structure may result in strengthening of the bone by inducing bone formation by osteoblasts and reduction of bone reabsorption by osteoclasts. We hypothesized that strontium-coated and antimicrobial-doped clay nanoparticles can be used as antimicrobial coatings, antimicrobial delivery vehicles, and osteoconductive and osteoinductive biomaterials. Sr when combined with calcium phosphate cement (CPC) can potentially integrate both antimicrobial and osteoinductive/osteoconductive properties. We coated halloysite (HNT) using strontium carbonate (SrCO3) to make Sr coated HNTs (SrHNT). We tested the antibacterial properties of SrHNT on Escherichia coli and Staphylococcus aureus by microtitration method. We assessed the potential cytotoxic effect of SrHNT on mammalian pre-osteoblasts cells (MC3T3-E1) using a Live/Dead cytotoxity assay and their potential proliferative effect on these cells using a BrDU proliferation assay. We successfully coated HNTs with strontium using a one-step benign coating method and not producing any toxic waste, in contrast to most HNT metal-coating methods. No cytotoxic effect was observed after MC3T3-E1 cells were exposed to SrHNTs and enhanced proliferation was also observed. Further testing of SrHNT is required to test the antibacterial and osteogenic properties within a bone defect animal model. If successful, embedding SrHNTs in calcium phosphate paste may enhance the osteoinductivity, osteoconductivity, and tissue formation properties of the calcium phosphate bone cement.

20 **Cell-Penetrating MK2 Inhibitory Peptide Blocks LPS-Induced Expression of Pro-inflammatory Cytokines in HepG2 Hepatocytes**

Ms. Tiffany Francis, Durina Dalrymple, Yaswanthi Yanamadala, Victor Carriere, Scott Poh, Audrey Kim, Paul Kim
Grambling State University, Louisiana Tech University

Mitogen-activated protein kinase-activated protein kinase 2 or MK2 plays an important role in inflammation. We synthesized and evaluated the functionality of two selective MK2 inhibitors: anti-inflammatory peptide (AIP-1) and AIP-1 conjugated to a novel cell-penetrating peptide (CPP-AIP-1). CPP-AIP-1 reduced the expression of CXCL8 and TNF in HepG2 human hepatoma cells challenged with lipopolysaccharides (LPS), whereas AIP-1 had no significant inhibitory effect. Our results demonstrate the application of a cell-penetrating peptide to enhance drug delivery in an in vitro model of liver inflammation.

21 **State Space Partitioning and Morphological Phylogenetics**

Ms. Courtney Grigsby, Tyler Tran, Basanta Khakurel, April Wright
Southeastern Louisiana University

Phylogenetic trees provide essential information to many facet of systematics and evolutionary biology. Accurate phylogenetic inferencing has become increasingly challenging as more complex data is introduced. This issue emphases the necessity for models of evolution that encompasses this data. Developed methods for estimating trait evolution, using molecular data examines changes in DNA sequences. These changes are bound to 4 different states, establishing a relatively standard approach for describing molecular changes. Morphological data presents contrasting issues because it possesses no such bounds. It is improbable to definitively know the number of states for a given [phenotypic] character. This can be attributed to commonly incomplete paleontological data-sets. Many inferencing techniques aim focus at expressing morphological traits as discrete characters. Utilizing discrete morphological data is advantageous considering its [quantitative] resemblance to that of molecular data, and the improve methods that accompany it. Moreover, unlike molecular data, when using morphological data we must consider occurrences of a trait can be analogous, that is the trait can arise from multiple independent evolutionary lineages. Incorrectly partitioning morphological characters by state space can lead to an inaccurate phylogeny. We seek to investigate the effects of model misspecification on phylogenetic inferences. Character data with varying trait states were simulated and modeled. These simulations were then used to estimate phylogenies with using the correct number of states, and with an incorrectly specified number of states. The results of this study will allows us to observe the degree in which the character state space can be subdivided while maintaining convergence of our analysis.

22 **Fusarochromanone as a Therapeutic for Prostate Cancer**

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Louisiana State University Shreveport, Louisiana State University Health Sciences Center Shreveport

Prostrate cancer has remained a significant human health problem in a majority of western countries. In the United States, it is the most common non-skin cancer and second leading cause of cancer related deaths in men. Androgen deprivation therapy has proven useful in the treatment of advanced prostate cancer (PCa). However, overtime the tumors become resistant to androgen deprivation and almost always progress to castration-resistant PCa (CRPC). Activation of the Wnt/β-Catenin signaling pathway and upregulation of androgen receptors have been implicated in the progression of PCa to CRPC. Additionally, dysfunction in the autophagy cell cycle in cells is associated with PCa progression and survival. Fusarochromanone (FC101) is a small flavonoid molecule shown to have anti-cancer effects in several types of cancer. The goal of this project is to observe the effect of FC101 in PCa. Primary epithelial cells derived from normal human prostate tissue and cancerous prostatic cell lines were treated with various concentration of FC101. Cell proliferation assays and

luciferase assays were performed. Results showed that FC101 displays potent anti-proliferation activity in PCa. Specifically, FC101 treatment of PCa cells induces G1 phase cell cycle arrest. Additionally, it was found that FC101 treatment suppressed the activity of Wnt/beta-Catenin signaling in PCa cells thus resulting in reduced PCa proliferation. Finally, PCa cells treated with FC101 resulted in down-regulation of autophagic biomarkers. This was in comparison to PCa cells treated with chloroquine as a control. From our results we conclude that FC101 causes cell cycle arrest, decreased cancer cell proliferation, and down-regulation of autophagic biomarkers in PCa.

23 Leveraging Hi-C and Whole Genome Shotgun Sequencing Data for Double Minute Chromosome Discovery

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Double minute chromosomes are acentric, extrachromosomal circular fragments of DNA that are frequently observed in the tumor cells of various cancer subtypes. They are highly amplified and contain oncogenes and drug resistance genes, making their presence a challenge for effective cancer treatment. Algorithmic discovery of double minutes (DM) can potentially improve bench-derived therapies for cancer treatment. A hindrance to this task is that DMs evolve, yielding circular chromatin that shares segments from progenitor double minutes. This creates distinct double minutes with overlapping amplicons, making accurate DM structure prediction a challenge. Existing DM discovery algorithms use whole genome shotgun sequencing in isolation; this can potentially classify DMs incorrectly if distinct DMs have overlapping amplicons. In this study, we describe a pipeline named 'HolistIC' that can predict double minutes in tumor genomes by integrating whole genome shotgun sequencing (WGS) and Hi-C sequencing data. Using WGS and Hi-C in tandem resolves ambiguity in double minute structure prediction that exists when using WGS data alone. We expect HolistIC to outperform existing methods since they only use WGS data in isolation and thus cannot account for potential ambiguities in double minute structure.

24 Role of MED12, Notch1, Notch3 in hASC Cell State Regulation and their Integrated Use in Public Educational Materials

Ms. Rebecca Hodnett
Louisiana Tech University

Adult stem cells offer significant therapeutic potential, however, to harness their medically relevant properties, more basic research must be performed. Cell state and differentiation of stem cells is determined by interactions of signaling pathways, chromatin modifiers, and transcription factors working to regulate cell-type specific gene expression profiles. I am currently investigating the role of Notch signaling and transcriptional cofactor, MED12, to

understand the relationship between various regulatory mechanisms that determine cell fate. The MED12 subunit of the Mediator complex and the Notch signaling pathway are both known to influence hASC self-renewal. We will investigate physical relationships between MED12, Notch1, and Notch3 intracellular domains and use siRNA mediated knockdown, to determine the effect that decreased MED12 expression has on Notch1 and Notch3 intracellular domain activity. Understanding the interaction of MED12, Notch1, and Notch3 and their influence on self-renewal will increase understanding of hASC cell fate for applications in regenerative medicine. To advance support for stem cell research, public education of the basic science and medical relevance of stem cells must also be addressed. An interactive children's book is currently being developed and will be employed to integrate basic science research and stem cell concepts inside and out of formal educational facilities; specifically designed to communicate fact-based stem cell content, address misconceptions, and promote positive engagement and interest. Together, this project will elucidate regulatory mechanisms involved in the interaction of the Notch signaling pathway with MED12 in hASC self-renewal while providing educational materials for continued support of stem cell research and applications.

25 Novel nanocarrier based on Vitamin E derivatives for nucleic acid delivery

Mr. A K M Nawshad Hossian, Seetharama Jois, and George Mattheolabakis
University of Louisiana at Monroe

The major challenge in the clinical translation of nucleic acid-based approaches is their stability against nucleases in vivo. Novel viral and nonrival delivery methodologies are being studied, but toxicity, immunogenicity, lack of biocompatibility, and increased cost have limited their development. Here, we present our work on a novel polymeric system based on vitamin E for the safe delivery of nucleic acids. We developed novel polymeric conjugates between α-tocopherol (Toc), Polyethyleneimine (PEI), and Polyethylene glycol (PEG), referred to as TPP. When these Vitamin E derivatives are placed in water, Toc forms a hydrophobic core, surrounded by a positively charged polyethyleneimine corona. Finally, at the distal end, the polyethylene glycol attachment will enhance the solubility and endow the carrier with prolonged circulation. Through a panel of synthesized polymers, we identified and worked on the 1:1:1 molar ratio of Toc:PEI:PEG, referred to as TPP111. We confirmed the conjugation and synthesis of TPP111 with NMR, FTIR, and DSC. The polymer self-assembled in water and generated globular shaped structures of ~90 nm, which was confirmed by DLS and TEM. The TPP111 polymer generated low toxicity with or without nucleic acids, while complexed with plasmids at a low N/P ratio (i.e., ~7). More importantly, the TPP111 polymer protected the complexed luciferase-expressing plasmid from enzymatic degradation, and the TPP111-plasmid complexes induced strong transfection in lung cancer cell lines, comparable to PEI. Cy5.5-tagged TPP111 complexes with plasmid were rapidly uptaken by cancer cells in vitro, indicating strong colocalization with endosomes. After systemic administration in tumor-bearing nude mice, the Cy5.5-TPP111-plasmid complexes reached the tumor site, with a preferential accumulation at the tumor area vs. other organs. Overall, the TPP polymer is a novel molecule that can safely deliver nucleic acids in vitro and in vivo, which merits further

evaluation.

26 The role of MED12 in adipogeneisis of human adipose stem cells (hASCs)
Ms. Onyekachi Idigo, Jamie Newman
Louisiana Tech University

The role of MED12 in adipogenesis of human adipose stem cells (ASCs) Human adipose stem cells (hASCs) are found in the adipose tissue of the body and are multipotent and self-renewing. Today, there is a growing interest in understanding adipogenesis due to the high rate of obesity in the world. It is not only the environment that determines cell fate, but how the environment, internal signaling cascades, and genomic regulatory elements work together to drive lineage commitment. The Mediator complex is one of the factors that is critical to the proper regulation of cell state as it bridges protein interactions on the genome allowing signaling pathways to direct gene expression. MED12 constitutes part of the Mediator kinase domain and has been shown to play a major role in stem cell regulation through interactions with CDK8 and Cyclin C. Mutations in MED12 lead to developmental disorders and certain malignancies, however, to date, specific roles of Mediator and MED12 in cell state regulation remain unclear. Therefore, this study will investigate the role of MED12 in the Mediator complex and kinase domain in order to better understand transcriptional control of adipogenesis in hASCs. We will investigate physical relationships between MED12 and adipogenic markers as well as use siRNA mediated knockdown, to determine the effect that decreased MED12 expression has on key adipogenic markers. At the end of the study, we will better understand the interaction of MED12 with adipogenic transcription factors and other subunits of the Mediator complex, providing a clearer picture of how adipogenesis is regulated. Key words: Adipogenesis, Mediator complex, MED12, Transcription factors

27 The Effects of Incorrect Character States in Phylogenetic Analyses
Mr. Basanta Khakurel, Dr. April Wright, Courtney Grisby, Tyler Tran
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Phylogenetic trees establish a historical context for the study of organismal form and function. Most phylogenetic trees are estimated using a model of evolution. For molecular data, modeling evolution is often based on biochemical observations about changes between character states. For example, there are four nucleotides, and we can make assumptions about the likelihood of transitions between them. By contrast, for morphological characters, we do not know a priori how many states there are, as both extant sampling and the fossil record may be highly incomplete. For a given character, the state space may be larger than what has been observed in the sample of taxa collected by the researcher. On the other hand, incorrectly partitioning characters by state space may also lead to model misspecification. We simulated character data with varying numbers of character states. We then modeled the data to estimate phylogenies with the correct number of character states and an incorrect number of character states. We simulated data using a tree of Formicidae.

We used this group because the ants have a long and rich fossil record, but there are still gaps in that fossil record. Therefore, it is likely that for some characters, we have not observed all the states. The results of this study will allow us to quantify how serious this observer bias is likely to be.

28 Cell-penetrating MK2 Inhibitory Peptide Blocks Proinflammatory Cytokines in HepG2 Hepatocytes

Dr. Paul Kim, Tiffany Francis, Durina Dalrymple, Audrey Kim, Yaswanthi Yanamadala, Victor Carriere, Scott Poh
Grambling State University, Louisiana Tech University

Mitogen-activated protein kinase-activated protein kinase 2 or MK2 plays an important role in inflammation. We synthesized and evaluated the functionality of two selective MK2 inhibitors: an anti-inflammatory peptide we call AIP-1 and AIP-1 conjugated to a novel cell-penetrating peptide (CPP-AIP-1). CPP-AIP-1 reduced the expression of CXCL8 and TNF in HepG2 human hepatoma cells challenged with lipopolysaccharides (LPS), whereas AIP-1 had no significant inhibitory effect. Our results demonstrate the application of a cell-penetrating peptide to enhance drug delivery in an in vitro model of liver inflammation.

29 Phylogenetic Posterior Predictive Assessment on a Fossilized Birth-Death Model

Ms. Christina Kolbmann, Jeremy Brown, April Wright
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Formicidae species are a model group for studying diversification, because of their extensive collection records, geographic range, social complexity, and pathogen-like evolution. Large molecular, morphological, and fossil age datasets were integrated in a Fossilized BirthDeath (FBD) analysis to test the flexibility of Phylogenetic Posterior Prediction to assess the fit of diversification models and time-stratified datasets. A RevBayes tutorial, 'Introduction to Posterior Prediction' was also created for introductory comprehension and non-phylogenetic analysis.

30 Hsp90 inhibitors induce the unfolded protein response in bovine and mice lung cells

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University of Louisiana at Monroe

The unfolded protein response element protects against endoplasmic reticulum stress and delivers protection towards potentially harmful challenges. The components of this multi-branch molecular machinery, namely the protein kinase RNA-like ER kinase, the activating transcription factor 6, and the inositol-requiring enzyme-1α; expand the endoplasmic reticulum capacity to support cellular function under stress conditions. In the present study, we employed bovine pulmonary aortic endothelial cells and mice to investigate the

possibility that the Hsp90 inhibitors Tanespimycin (17-AAG) and Luminespib (AUY-922) exert the capacity to trigger the unfolded protein response. The induction of the unfolded protein response regulators immunoglobulin heavy-chain-binding protein, endoplasmic reticulum oxidoreductin-1alpha; and protein disulfide isomerase was also examined. It appears that both inhibitors capacitate the induction of the unfolded protein response element in vitro, since lung cells exposed to 1, 2 and 10 µM of 17-AAG or AUY-922 for 4, 6, 8, 16 and 48 h demonstrated increased levels of those proteins. Similar events occurred in the lungs of mice treated with AUY-922. Thus, our study demonstrates that Hsp90 inhibition triggers the activities of the unfolded protein response, and suggests that this molecular machinery contributes in the protective action of Hsp90 inhibitors in the lung microvasculature. The present study was supported by the R&D, Research Competitiveness Subprogram (RCS) of the Louisiana Board of Regents through the Board of Regents Support Fund (LEQSF(2019-22)-RD-A-26) and the Institutional Development Award (IDeA) from the National Institute of General Medical Sciences of the National Institutes of Health (5 P20 GM103424-15 and 3 P20 GM103424-15S1) to N.B. (PI).

31 Targeted Delivery of Doxorubicin Liposomes for Her-2 Positive Breast Cancer Treatment

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Doxorubicin is one of the most potent drugs used widely for breast cancer treatment. The adverse side effects and toxicity caused by the non-targeted delivery of doxorubicin has emphasized the demand of emerging a targeted delivery system. The goal of this study is to enhance the delivery of doxorubicin by formulating an aptamer-labeled liposomal nanoparticle delivery system that will carry and deliver doxorubicin specifically into Her-2+ breast cancer cells. 12 liposomal batches were prepared using different saturated and unsaturated lipids such as DOPC, DPPC, POPC and HSPC by thin film hydration. The liposomes were characterized for particle size and zeta potential. Ammonium sulphate gradient method was used to passively load DOX into the liposomes. Scanning electron microscopy (SEM) was used to investigate the morphology of liposomes. In vitro cytotoxicity assay was done to evaluate the effect of DOX and DOX loaded liposome on MCF-7 and SKBR-3 breast cancer cells. Uptake studies were done with batches F1, F5, F8 and F12 by fluorescence microscopy and flow cytometry. Results: The formulations, F1 through F12, had a small particle size of less than 200 nm and a high entrapment efficiency of about 88±5%. The best formulation, F5, had a particle size of 101±14 nm, zeta potential of +5.63±0.46 mV and entrapment efficiency of ≈93%. The cytotoxicity studies show that the DOX loaded liposomal formulations are more effective in killing cancer cells than the free DOX in both MCF-7 and SKBR-3 cells. The uptake studies show a significant increase in the uptake of the aptamer-labeled liposomes (i.e. F5) by more than 60% into Her-2+ MCF-7 and SKBR-3 breast cancer cells compare to non-aptamer labeled nanoparticles. Aptamer targeted approach results in substantial reduction in the dose of DOX and improves the therapeutic benefits by promoting the target specificity.

32 Conjunctival microbiome in domestic cats is minimally altered in ocular surface disease

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Objective To determine the impact of ocular surface disease (OSD) on the conjunctival microbiome in domestic cats. Animals 38 normal cats and 43 cats with varying degrees of OSD. Procedures Conjunctival swabs were collected from each animal and clinical data recorded using an OSD scoring system. rDNA was extracted from swabs for Illumina MiSeq 16S sequencing. Assessment using QIIME2 was performed, with alpha (assessed with Kruskal-Wallis test) and beta diversity (assessed with PERMANOVA test) measured using 4 metrics each. Significance was set at $p < 0.05$. Results Five contaminated outlier samples (3 diseased animals and 2 normal animals) were removed from analysis. Alpha diversity using one metric (Pielou's evenness) showed differences between animals based on chemosis ($p=0.006$) and total eye disease severity score ($p=0.02$, $p=0.04$). No differences were detected for other disease variables for any of the other 3 alpha diversity metrics. PERMANOVA detected significant differences in only 1 beta diversity metric (Jaccard index) for animals with and without eye disease ($p=0.03$). No differences were detected for other disease variables for any of the other 3 beta diversity metrics. The relative abundance of microbial taxa was homogenous in almost all samples, regardless of OSD status. Mycoplasma spp. was detected in 7 animals with OSD and no normal animals. Conclusions and Clinical Relevance The presence of ocular surface disease minimally influenced the diversity of the feline conjunctival microbiome in this group of cats. The technique was able to identify Mycoplasma spp. in animals with ocular surface disease.

33 3D Printed Polymer Blend Nano-Composites Enhanced with Growth Factor Doped Halloysite Nanotubes

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Titanium is the industry standard for the manufacturing of surgical screws, pins, osteofixation devices, and stabilization plates. These titanium implants are used to fix and stabilize bones that have been broken or fractured with the goal to provide strength and function so that the injured bones may heal. While titanium is the most employed implant material used today, there are some adherent risks associated with its long-term implantation. In addition, it is bioinert, can lead to corrosion and often sees surface biofilm formation. We hypothesize that a poly-caprolactone, poly-L-lactic acid and poly-glycolic acid polymer composite containing halloysite nanotubes embedded with growth factors will be able to replace the bio-inert titanium devices with comparable strength and flexibility as well as resorbing as new bone growth begins. Transforming growth factor β3 serves as a mesenchymal stem cell recruiter and stimulus of cellular differentiation. Ultimately, the purpose of this medical implant is to stabilize a bone fracture, release growth factors that recruit stem cells which differentiate

into chondroblasts and osteoblasts when exposed to the aforementioned growth factors, and finally completely dissolve leaving newly formed bone and cartilage tissue. Successful completion of this project may provide an alternative treatment option.

34 Investigating the Novel Protein-Protein Interaction between GleIF4A RNA Helicase and GleIF3i, a Member of Preinitiation Complex, in Primitive Eukaryote Giardia lamblia

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Giardia is considered as one of the earliest branching Eukaryotes and has become a model organism for gaining insight into the evolution of various cellular processes, including eukaryotic translation initiation. The primary differences between Giardia translation initiation and other mammalian cells are centered around Giardia's lack of 3 key translation initiation factors: eIF4B, eIF4H, and eIF4G. Both eIF4B and eIF4H are thought to stimulate the affinity of the RNA helicase eIF4A for RNA, increase its activity, and prevent reannealing of unwound ssRNA. eIF4G is a scaffolding protein that connects the eIF4F complex to the subunits of the PIC. Therefore, in the absence of eIF4G, it is not clear as to how the PIC and RNA helicase are recruited to the 5' end of mRNA in Giardia. A novel protein-protein interaction (PPI) was discovered between GleIF4A and the subunit GleIF3i, indicating a possible way for GleIF4A to be recruited to the PIC. Analysis of the GleIF4A protein structure was integrated with ZDOCK modelling to predict potential docking conformations between GleIF4A and GleIF3i. The model found 10 amino acid residues where GleIF4A and GleIF3i are potentially interacting. These results were used to create several mutant GleIF4A constructs via site-directed mutagenesis, and their effects were analyzed in a yeast 2-hybrid system. Of the 7 mutant GleIF4A constructs that were successfully cloned into yeast expression vectors and assayed on selective media, 3 showed complete loss of interaction with GleIF3i. Interestingly, all 3 contained mutations within the N-terminal domain, and C-terminal domain mutations resulted in no visible loss of interaction with GleIF3i. The novel PPI discovered between members of Giardia lamblia's translational machinery, GleIF4A and GleIF3i, was validated further through reverse genetics approaches. By ZDOCK-guided mutation of amino acids in the N-terminal domain of GleIF4A, there was a loss of interaction between these two proteins.

35 Reverse Phase Protein Array Analysis of FC101m Treated TNBC and ATC Cell Lines

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Fusarochromanone (FC101m) is a novel, small molecule fungal metabolite that demonstrates potent inhibitory effects toward numerous cancer cell lines in-vitro, but the effects are limited in-vivo. However, the exact mechanism of action is unknown so the ability to synthesize effective derivatives are limited. The primary objective of this research is to use reverse phase protein assay (RPPA) analysis to deduce possible mechanisms of action of

FC101m induced apoptosis in triple negative breast cancer (TNBC) and angioplasty thyroid cancer (ATC) cell lines. YM155, an ATC drug currently on the market, was analyzed alongside FC101m for compound effectiveness comparison. RPPA analysis provided over 262 proteins validated using normalized linearization in both cell lines that were affected by FC101m. In the TNBC cell line, FC101m was found to significantly influence: JNK2 and Shc_pY317. In the ATC cell line, FC101m significantly effects FoxM1, Axl, and Myosin-IIa pS194. Utilizing the proteins significantly influenced by FC101m, a potential mechanism of action can be established in order to synthesize successful derivatives.

36 Synthesis and Anticancer Activity Evaluation of Pyrazole and Pyrazolone Derivatives

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University of Louisiana at Monroe, Louisiana State University

Lung cancer is by far the leading cause of cancer-related death among both men and women; more deaths caused by lung cancer every year than by breast, prostate, and colon cancer combined. The two major forms of lung cancer are non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC), and NSCLC comprises approximately 85% of all lung cancers. Currently we are working on synthesis and biological evaluation of pyrazole and pyrazolone based small molecules as potential anticancer agents. We have recently identified a set of compounds exhibiting anticancer activity particularly towards non-small cell lung cancers (NSCLC). Until now, treatment of NSCLC has had limited success and new therapeutics are desperately needed. We have synthesized several derivatives of lead molecule(s) and evaluated their in-vitro antiproliferation activity using Celltiter Glo assay. A few compounds showed good potency against two cancer cell lines i.e. human lung carcinoma (A549) and human adenocarcinoma (NCI H522). In addition to that, we performed PARP inhibitor analysis and cell cycle analysis, and obtained data from kinase profiling studies. We will present the data and results from our synthetic approaches and biological assays.

37 Purification of Alkaloids from Medicinal Plant Camptotheca acuminata, the Producer of Anticancer Camptothecin

Dr. Vahid Nasirian, Jacqueline Dennis, Emily Rabalais, Vonny Salim
Louisiana State University Shreveport

Camptothecin is a monoterpenoid indole alkaloid that exhibits anti-tumor activity obtained from Camptotheca acuminata (Cornales), a tree native to Southern China. At present, semi-synthetic water-soluble camptothecin analogues, Food and Drug Administration (FDA)-approved Topotecan and Irinotecan, are used as chemotherapeutic agents in the clinic. We hypothesized that C. acuminata also accumulate alkaloids with important pharmacological activities that need to be purified to investigate their mode of action as well as elucidation of camptothecin biosynthetic pathway. In this work, we separate the methanol extracts of root and young leaves from C. acuminata plant. The purification procedure was carried out by

column chromatography to produce fractions which were then analyzed by high performance liquid chromatography (HPLC) coupled to UV with fluorescence detectors and HPLC-Mass Spectrometry (MS). The findings based on this robust purification method demonstrate a remarkable difference in the constituents between root and leaf tissues. The metabolite profiling of alkaloids provides more insights into camptothecin biosynthetic machineries while the purified metabolites will be tested for their anticancer activities and used as substrates in the biochemical characterization of novel biosynthetic genes.

38 Analysis of amino acids residues involved GleIF4E2 interactions with GleIF2beta in Giardia lamblia

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Giardia is a unique model eukaryote because it lacks 3 key translation initiation factors, eIF4G, eIF4B, and eIF4H. Translation initiation factor eIF4G is known to interact with RNA helicase eIF4A and cap-binding protein eIF4E. This leads to recruitment of the preinitiation complex to the 5' cap and subsequent translation of mRNA. Translation initiation factor eIF4G binds to the PolyA binding protein 1 thus the messenger RNA's poly A tail. Translation initiation factor eIF4H stimulate the initiation of protein synthesis at the level of mRNA unwinding. Giardia like other Eukaryotes do have translation initiation factor eIF4E2, but not EIF4G. The mechanism of ribosome recruitment to mRNA in the absence of eIF4G is less understood in Giardia. A recent novel interaction was discovered between GleIF4E2 and GleIF2beta. ZDOCK computer modeling of GelIF4E2-GleIF2beta was used to identify various amino acid residues where these two proteins could be interacting. To assess the role of these amino acids we performed site directed mutagenesis followed by assaying through yeast-two hybrid. Of the seven amino acid residues that were tested we were able to identify three residues, L12, F45, and F46, that affected the interaction of 4E2 and 2beta. The ZDOCK program was able to identify three different types of mutations that can prevent the protein interactions of 2beta and elF4E2, however, the disruption of the interactions will be further tested.

39 Comparing Treatment of Adipose Stem Cells for the Differentiation of Clinically Relevant Cells

Dr. Jamie Newman, Haley Barnett, India Pursell, Mary Caldorera-Moore, Bruce Bunnell
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Human adipose-derived stem cells are the easiest adult stem cells to access, harvest, and isolate, providing the largest supply of autologous stem cells for clinical application. As stem cells, hASCs have the ability to self-renew, differentiate, and suppress inflammation. In clinical trials, these cells are being isolated and expanded to treat a similar set of health conditions with a more targeted interest in regeneration. In addition to these on-going clinical studies there is also research being performed to generate tissue patches that can aid

in the repair of significant injury to tissue including heart and skeletal muscle. With the interest in using isolated stem cells in cell-based treatments and in areas of tissue engineering and regenerative medicine it is critical that we find efficient and clinically relevant methods for maintaining and differentiating stem cells. This project attempts to address deficiencies in tissue and cellular biomanufacturing pipelines associated with hASCs through the assessment of physical environment and cell behavior. To work towards creating cells that can reliably be used in the clinic and generate functional myogenic tissue we are evaluating hASC long-term replicative potential in physiologically relevant environments as well as assessing the influence of these environments on cellular memory. Together these studies will provide critical information and guidelines for the long-term maintenance of self-renewing, multipotent, and clinically relevant adult stem cells.

40 **Autism Spectrum Disorder in Zebrafish After Exposure To Four Organophosphate Pesticides**

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The objective of this study were to determine whether organophosphate pesticides altered behavior of the zebrafish (Danio rerio) in order to further understand the mechanism of action of autism in children when exposed to this class of pesticides. An increased association between this disease and exposure has been identified in multiple epidemiology studies. To determine if there is a correlation, 48-hour post fertilization zebrafish were exposed to chlorpyrifos, parathion, malathion, and methyl-parathion for five days at 0, 0.01, 0.1, and 1 µM. At the end of the exposure period, animals were subjected to the following behavioral and social experiments: larvae activity, light/dark activity, startle response, and 3-point tracking. The two chemicals with the most significant effects on behavior and sociality were chlorpyrifos and parathion. Future studies should include alterations in the timing of exposure as well as the age at which zebrafish embryos and larvae are exposed.

41 **Charge Transfer between Perovskite Nanocrystals and Carbon Nanotubes**

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Lead halide based perovskite nanocrystals (PNCs) functionalized with single walled carbon nanotubes (PNC@CNT) were prepared. MAPbX3 PNCs are very bright in luminescence, but quenching happens in the presence of CNTs. Morphological characterizations and life time studies are proceeded to investigate charge transfer studies. This is intended for biosensing.

42 **Methods and Techniques for Myogenic Differentiation of Human Adipose-Derived Stem Cells**

Ms. Nellie Perez, Summer Adams, Laura Lee, John Bradley Cart, Haley Barnett, Mary Caldorera-Moore, Jamie Newman
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Human adipose-derived stem cells (hASCs) are multipotent stem cells that have the potential to self-renew and differentiate. In an effort to optimize conditions for the myogenic differentiation of adult stem cells and improve their potential in the clinic, we cultured hASCs on collagen-coated tissue culture plates using two different medias with varying amounts of fetal bovine serum (FBS). Following six weeks of myogenesis, cells were characterized by cellular morphology, protein expression, and transcription of myogenic specific genes. Staining and immunofluorescence (IF) are used to determine the success of each culture surface and media by allowing for the visual and qualitative evaluation of myogenic protein expression. Immunofluorescence using the antibodies for MYOD and myosin will be used to qualitatively assess the expression of these myogenic transcription factors and proteins respectively to evaluate differentiation. Phalloidin is used to visualize actin filaments, while DAPI binds to adenine-thymine rich areas in DNA to visualize cell nuclei. To quantitatively analyze our cultured hASCs, we use quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR). Here, RNA is extracted from cells and reverse-transcriptase is used to synthesize complementary DNA (cDNA). The cDNA is then used as a template for quantitative PCR which utilizes fluorescent dyes to record amplification and provide more accurate data of transcript levels of myogenic markers such as myod, myf5, and myogenin. By using these cell culture and molecular techniques, we are able to differentiate hASCs and characterize the efficiency of myogenesis under various conditions. Conclusions drawn from this research contribute to regenerative medicine research currently seeking improved methods for the generation of functional muscle tissue.

43 **Investigation of transcriptional control in directing cell fate**

Ms. Claire Peterson, Foram Patel, Lauryn Cain
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Cell fate is driven by changes in gene expression which are the result of external cues, endogenous signaling pathways, and transcriptional machinery all working together. Human adipose-derived stem cells (hASCs) are adult stem cells derived from adipose tissue that are used in clinical research because they can be easily extracted, are multipotent, are able to self-renew, and have natural immunomodulatory capabilities. Culturing hASCs in the lab allows for the in-depth study of cell fate determination with the ability to manipulate the environment and easily assay changes in cell fate, transcription, and protein expression. Our project is primarily interested in investigating how protein expression levels of the four subunits of the Mediator kinase domain affect adipogenesis of hASCs. We are using cell culture to grow and examine changes in cell behavior over seven days during which cells are stimulated to undergo adipogenesis. Gene expression is assessed through the collection of

RNA which is then used to synthesize cDNA, that is analyzed using gene specific primers to measure relative transcript levels using both end-point and quantitative RT-PCR. Protein expression is quantified and analyzed through a Bradford Assay and Western Blot using specific antibodies to assess Mediator protein levels. By using cell culture, directed differentiation, qRT-PCR, and western blots we are able to understand the transcriptional processes that directs hASC fate, creating a strong foundation for future research to investigate novel therapies for cancers and other disorders.

44 **Reversal of the Maxi-K channel antagonist penitrem A neurotoxicity by the olive oil lignans via the JAK/Stat pathway**

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Penitrem A, PA, is an indole diterpene mycotoxin from several fungal species. PA acts as a selective Ca++-dependent K-channels (Maxi-K, BK) antagonist in brain, causing motor system dysfunctions, e.g., tremors, seizures, hyperthermia, and ataxia. However, its molecular mechanism at the peripheral nervous system (PNS) is still ambiguous. Myelination of PNS axons is carried out by Schwann cells, which originate from the neural crest. The Mediterranean diet key ingredient extra-virgin olive oil (EVOO) provides a variety of minor bioactive and neuroprotective phenolic secoiridoids and lignans. (+)-Pinoresinol (PN) and (+)-1-acetoxypinoresinol (AP) are naturally occurring lignans in EVOO with diverse biological activities including anticancer, antioxidant, anti-inflammatory, and anti-allergic effects. PA inhibited the viability of Schwann cells, in vitro, with an IC50 of 22.6 µM. The role of interferons (INF) in promoting apoptosis of Schwann has already been documented. Our results suggest that PA neurotoxicity molecular mechanism is via distortion of the JAK/Stat pathway. PA selectively induced the INF-γ-dependent activation of STAT1 pathway in vitro in Schwann cells and in vivo in Swiss albino mouse sciatic nerves. The goal of this study was to discover natural products that can reverse the neurotoxicity of PA for future food safety application. Screening of EVOO phenolics for ability to reverse PA toxicity on Schwann cells revealed PN and AP as potential hits. In Swiss albino mouse model, AP significantly minimized the fatality after intra-peritoneal administration of PA fatal doses. A study of behavioral attitudes in Swiss albino mice demonstrated the ability of AP to counteract PA neurotoxic effects and normalize most biochemical factors by modulating the STAT1 pathway. The olive lignans are novel leads useful for use to control and prevent the Maxi-K-targeting food contaminating indole alkaloid mycotoxins neurotoxicity.

45 **How to Train Your AI: Quantification of R-Loop Expression in Anaplastic Thyroid Carcinoma using Immunohistochemistry and Automated Cell Segmentation Software**

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Anaplastic Thyroid Cancer (ATC) is one of the most aggressive forms of thyroid cancer. Evidence from our lab suggests that R-loops may play a prominent role in ATC cell death. The process of manually quantifying r-loops can be physically taxing for the user. The Mantra Multispectral Imaging system incorporates multispectral imaging and the inForm™ Analysis software. Here we quantitatively analyzed R-loops expression in ATC cell lines using immunofluorescence and the Mantra ™ and inForm ™ systems. Comparisons were made between the accuracy, sensitivity, and specificity of the AI-generated masks to manually generated ones. The results show that the inForm™ software may be used to automate the process of detecting R-loops in ATC cell lines.

46 **Assessment of LRP1-mediated uptake of cationic peptides as potential therapeutic vehicles in brain microvascular endothelial cells**

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The delivery of biotherapeutics into the brain for the remediation of specific Central Nervous System (CNS) disorders like neurodegenerative disorders is impeded by their suboptimal blood-brain barrier (BBB) penetration. Unlike small lipophilic molecules, larger molecules such as proteins and nucleic acids cannot generally penetrate though the brain's primary structural barrier- the brain endothelial cells in the capillaries of the brain and spinal cord, which restricts their paracellular and transcellular transport to the brain parenchyma. As such, there is a need for multiple drug candidates and modes of delivery that can efficiently transport biotherapeutics across the BBB. In this study, we used primary rat brain microvascular endothelial cells (BMVEC) to visualize the intracellular accumulation and localization of fluorescently-tagged cationic peptides in vitro through fluorescence microscopy. Receptor-mediated uptake was studied through peptides employing the low-density lipoprotein receptor-related protein 1 (LRP1) for transcytosis. We studied the cellular uptake of L57 - the first artificial LRP1-binding peptide with BBB permeability, together with two other peptides- Angiopep-7 and R8. Rat BMVECS were shown to be a good BBB model owing to their enhanced tight junction complexity and monolayer tightness. We also quantified the uptake of various concentrations of these peptides observed that L57 peptides exhibited better cellular uptake as well as biocompatbility than A7 and R8 in vitro. These results potentially qualify the synthetic L57 peptide as a promising new candidate as a carrier to enable increase in effective therapeutic concentrations of CNS biotherapeutics in the brain, which would be a major advantage over prevailing therapeutics. Testing different modes of administration and covalently bound uptake of different therapeutics could potentially be used to further evaluate L57's pharmacokinetic properties.

47 **In Silico Analysis for Characterization of Glucosidases from Anticancer Alkaloid-producing Medicinal Plants**

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Alkaloid glucosidases(AGDs) involved in the biosynthesis of anticancer compounds, Vinca alkaloids from medicinal plant Catharanthus roseus have been known to be specific towards their substrate. Camptothecin has been considered as one the essential medicines with anti-tumorigenic properties by inhibiting DNA topoisomerase. Because the anticancer compounds are found in low amounts in medicinal plants, metabolic engineering approaches have been pursued to increase their productions in microbial systems. As part of this engineering effort, the specificity of enzymes, such as GDs can be altered to allow better efficiency during manufacturing and/or creating analogs of anticancer compounds. In this study, we compare a group of AGDs involved in anticancer camptothecin biosynthesis in medicinal plant Camptotheca acuminata and strictosidine glucosidases (SGD) from Catharanthus roseus and Rauwolfia serpentina. In-vitro enzyme assays have shown while C. roseus and R. serpentina SGD are very specific towards 21(S)-strictosidine, the C. acuminata GDs accept multiple isomers (both (R) and (S)) of alkaloid glucosides found as intermediates in camptothecin pathway. We aim to identify sequence discrepancies in the catalytic pockets and other key residues using homology modeling for better precision in engineering of camptothecin biosynthetic pathway. Molecular docking with homology model of various alkaloid glucosides from C. roseus, R. serpentina, and C. acuminata was conducted using Molecular Operating Environment (MOE). Specifically, residues of interest, such as glutamic acid and aspartic acid have been shown maintaining the interactions with the glucose moiety and further cleavage. Understanding the enzyme specificity of these AGDs from three-dimensional perspectives in-silico will assist the modulation required to engineer enzymes involved in the biosynthesis of anticancer compounds.

48 **Synthesis and inverse-docking assisted identification of flavonols as c-Kit, CDK2 and mTOR inhibitors for treating melanoma and non-melanoma skin cancer**

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Cutaneous melanoma and non-melanoma cancers are commonly diagnosed annually, with 3 million patients in the US alone. In 2019, American Academy of Dermatology reported an estimated 7,230 death cases. Currently, therapeutic options are associated with long-term adverse effects, low bioavailability, and increase resistance. A promising strategy for urgent patient benefit is to synthesize and characterize newer, safer and low-cost bioactive derivatives of naturally occurring dietary anticancer compounds/agent. In this study, 21 new chemically synthesized and characterized flavonol derivatives were evaluated for their anticancer activity against human melanoma (A375), and non-melanoma skin cancer (NMSC: A431) cells at concentration range (0-40 μM). Eleven of these compounds, significantly

decreased the proliferation of the cancer cells with minimal effects on normal cells (keratinocytes/melanocytes). Three of these compounds (i.e. F11, F19 and F20) displayed low micromolar anticancer activity with over 3-10 folds potency in the sequence F20>F19>F11>curcumin over fisetin, a parent anticancer flavonoid. Inverse-docking analysis of the 11 active compounds against 12 known targets suggested CDK2, mTOR, PI3K, EGFR, and c-KIT as major anticancer targets to be developed. Further evaluation of the 3 potent derivatives by wound closure, cell migration, and clonogenic assays demonstrated a dose-dependent effect. Western blot analysis reveal the downregulation of the overexpression of diverse melanoma and NMSC molecular targets including Akt, mTOR, p90RSK, p70S6K, STAT3, EGFR, and ERK1/2. This study identified three potent flavonol derivatives as lead compounds to be further characterized and develop as an anticancer agent.

49 **The Gateway for Metabolic Engineering: Functional Characterization of Alkaloid Glucosidases in Anticancer Camptothecin Biosynthetic Pathway**

Dr. Vonny Salim, Vonny Salim, Camaray Rouse, Vahid Nasirian, Jacqueline Dennis, Casey Cocherell, Emily Rabalais, Elahe Mahdavian, Phillip Kilgore, Urska Cvek, Hugh Nam, Xiuping Yu, Khalid El-Sayed, Daniel A. Jones, Dean DellaPenna
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Medicinal plant Camptotheca acuminata produces anticancer camptothecin, a monoterpene indole alkaloid (MIA) that has been widely used in chemotherapy treatments. While other MIAs such as anticancer vinblastine extracted from Catharanthus roseus are derived from iridoid secologanin to generate a single 3-alpha-(S) of the central intermediate strictosidine, C. acuminata produces multiple secologanic acid isomers that are utilized to synthesize (R) and (S) diastereomers of strictosidinic acid. These central intermediates are then used to generate multiple isomers of alkaloid glucoside intermediates until the late stages of camptothecin pathway. Our bioinformatic analysis of C. acuminata genomes and transcriptomes have allowed the identification of MIA biosynthetic genes. In this study, the biochemical characterization of four novel glucosidases from C. acuminata reveals different substrate specificity compared with C. roseus strictosidine glucosidase which strongly prefers 21(S)-strictosidine. C. acuminata glucosidases show varying affinities towards multiple alkaloid intermediates involved in camptothecin pathway. Further characterization of substrate binding and the active site of these glucosidases demonstrates the structural significance of their catalytic pockets to explain why C. roseus strictosidine glucosidase is more specific towards its substrate, compared to C. acuminata glucosidases. The functional characterization of these glucosidases also allows identification of other biosynthetic genes involved in camptothecin pathway to accelerate metabolic engineering efforts for more efficient production of anticancer drugs in microbial systems.

50 **The novel breast cancer recurrence preventive activity and single oral dose safety of the extra-virgin olive secoiridoid S-(−)-oleocanthal**

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Breast cancer (BC) recurrence represents a challenge for survivors who have had their primary tumors surgically excised and/or have completed radiation, neoadjuvant, or adjuvant therapeutic regimens. Current BC treatments do not reduce the risk of disease recurrence. About 70% of BC patients will subsequently relapse, which is usually metastatic and fatal. This clearly highlights the urgent need to discover novel effective recurrence inhibitors. Oleocanthal (OC) is a natural phenolic exclusive in extra-virgin olive oil. OC exerts bioactivities against diverse cancer types, inflammation, and neurodegenerative diseases. Herein we report the novel activity of daily oral OC (10 mg/kg) to prevent luminal B BC locoregional recurrence in a nude mouse xenograft model. We further report OC ability to inhibit tumor recurrence (TR) after the completion of a lapatinib neoadjuvant regimen. OC Inhibition of TR was associated with significant serum level reductions of the human BC recurrence marker CA 15-3. Mechanistically, OC treatment upregulated the epithelial marker E-cadherin and downregulated the mesenchymal marker vimentin in recurrent tumors compared to control. We also assessed the safety of OC oral single dose in Swiss albino mice following the OECD 420 protocol. Male and female mice (n = 10) were treated with single oral OC dose of 10, 250 and 500 mg/kg body weight. After 14 days of clinical observations, mice were sacrificed, blood samples and organs were collected and subjected to hematological, biochemical and histological examinations. The therapeutic OC 10 mg/kg oral dose appears to be without adverse effects. Further, 250 mg/kg OC, p.o., is suggested as a possible upper dose for preclinical studies in the future. Collectively, the results of our studies highlight the potential of OC as a novel nutraceutical with good safety degree for long-term use by BC survivors to prevent disease recurrence and metastasis.

51 **Design, synthesis, and evaluation of grafted peptides/peptidomimetics for the inhibition of protein-protein interactions of EGFRs in osteosarcoma**

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The objective of this project is to understand the role of homo and heterodimerization of epidermal growth factor receptors (EGFRs) in osteosarcoma (OSA) and to design stable peptide-like molecules which will inhibit this protein-protein interaction. In this project, we proposed to inhibit the protein-protein interactions using novel grafted cyclic peptides by targeting EGFR proteins in OSA. Based on our previous studies, we have confirmed that the small cyclic peptides that were grafted with a peptidomimetic, inhibit the interactions of EGFR with HER2 and HER3 in human non-small cell lung cancer (NSCLC) both in in-vitro and in-vivo models. OSA is known to express EGFR-family proteins. Hence, we extended our studies to OSA cell lines that express EGFR proteins. Therefore, our proposed aim was to

understand the role of homo and heterodimerization of extracellular domains of epidermal growth factor receptors (EGFRs) in OSA and its inhibition by grafted peptides. We designed, synthesized grafted cyclic peptides and evaluated the cell viability in OSA cells that express EGFR-family proteins. Further, we evaluated the EGFR/HER2/HER3 protein expressions and assessed the molecular mechanism of inhibition of protein-protein interaction in human and canine OSA. To understand the immunogenicity of the peptides, a splenocyte proliferation assay was performed in an animal model, which suggests that our peptide was non-immunogenic in animals. These preliminary studies indicated that the grafted cyclic peptide showing promising results to inhibit the dimerization of EGFRs in OSA, hence they can have the potential to be developed further into therapeutic agents.

52 Novel pH-sensitive liposome formulation containing doxorubicin-peptidomimetic conjugate targeting HER-2 positive cancer cells for the enhancement of compound stability and therapeutic efficacy

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Liposome formulation has special size-dependent properties to effectively accumulate in the tumor microenvironment through leaky vasculature while maintaining the stability of the compound. A novel doxorubicin-peptidomimetic conjugate (C5-DOX) containing pH-sensitive liposomal formulation (PSC5-DOXL) targeting HER-2 positive cancer cells was prepared to cargo the compound while maintaining C5-DOX stability and after selective accumulation in the tumor microenvironment, release the C5-DOX conjugate in an acidic environment. PSC5-DOXL formulation was finalized after determining optimum drug:lipid ratio for effective pH-sensitive release property for the C5-DOX from the formulation. Physicochemical properties for PSC5-DOXL such as particle size, polydispersity index, zeta potential, and entrapment efficiency were found in desirable level such as 170.3 ± 3.8 nm, 0.209 ± 0.016, -24.6 ± 4.7 mV and 88.4 ± 1.5 % respectively. In-vitro stability of the PSC5-DOXL formulation was measured in 4oC as well as in human serum which indicated stable formulation in both experiments in terms of particle size of liposome and C5-DOX stability. In-vitro release study showed increased C5-DOX release within 2 hours in acidic condition while maintaining substantial difference with physiological pH up to 8 hours. In-vitro microscopy of the PSC5-DOXL formulation showed increased C5-DOX uptake in BT474 (HER-2 overexpression) cells with increased concentration from 1 µM to 3µM observed with DOX fluorescence. Antiproliferative assay of PSC5-DOXL formulation also suggests the formulation has low micromolar level activity against HER-2 positive cancer cells. These results suggest a promising stimuli-responsive formulation containing doxorubicin-peptidomimetic conjugate for selective and efficacious treatment targeting HER-2 positive cancers with minimizing off-target toxicity.

53 Optimization of Taste-Masked (-)-Oleocanthal Effervescent Formulation with Potent Breast Cancer Recurrence Suppressive Activity

Mrs. Afsana Tajmim, Afsana Tajmim, Abu Bakar Siddique, Khalid El Sayed
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S-(-)-Oleocanthal (OC), a monophenolic secoiridoid exclusively found in extra-virgin olive oil (EVOO) with potential bioactivties against inflammation, neurodegenerative diseases, and many malignancies, especially breast cancer (BC). The oral delivery of OC is challenging because of its irritative, bitter, and pungent taste and exceptional chemistry, including two reactive aldehydes, phenolic, and ester groups. The irritative sensation at the oropharynx caused by OC consumption is due to the activation of TRPA1. The objective of this study was to develop an effervescent formulation of OC with an effective CO2-induced masked taste maintaining the efficacy against the luminal BC. Several ratios of acid and carbonate sources were screened, and five effervescent formulations EF1-EF5 were selected and prepared based on their pH and effervescence time. OC formulations were characterized using differential scanning calorimetry, FT-IR spectroscopy, and scanning electron microscopy. Based on physical characteristics and improved OC release, formulation EF-2 was selected for subsequent studies. EF-2 showed effective OC taste masking, as suggested by electronic artificial tongue and mouse preference tests. EF-2 suppressed more than 70% of the hormone and HER2-positive BT-474 BC cell growth in a nude mouse xenograft model. EF-2 also demonstrated significant inhibition of BT-474 tumor cell locoregional recurrence after primary tumor surgical excision. EF-2-treated mouse sera had significantly reduced level of the human BC recurrence marker CA 15-3, versus placebo control group. OC formulation EF-2 is a prospective nutraceutical for the control and prevention of luminal BC progression and recurrence.

54 Pentachlorophenol-Mediated Induction of Inflammatory Responses In Alveolar Epithelial And LiverCarcinoma Cells

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Pentachlorophenol (PCP) was a widely used organochlorine pesticide in the U.S. for a long time. Currently it has been characterized as a restricted-use pesticide and established as a liver carcinogen by the EPA. It is now clear that PCP is an environmental toxicant that can be easily absorbed through the skin and lungs. But despite these evidences, the exact molecular mechanism affected by acute exposure to PCP is yet to be explored. Considering this, we intended to study the effects of PCP challenge on inflammation and ROS production in human lung adenocarcinoma cells with type II epithelial characteristics (A549) and liver carcinoma (HepG2) cells. We challenged human lung and liver epithelial cells with varying concentrations (1-10µM) of PCP for 24-hr duration and studied the transcriptional and transnational expression of proteins involved in immune and inflammatory response. We found an increase in the levels of NADPH oxidase (NOX) subunits- NCF-1 and NCF-2- on PCP-challenge in both models. NOX proteins are responsible for superoxide generation and have

an important role in innate immunity. We further demonstrated an increase in the expression of transcription factor-NF-kB; and mitogen-activated protein kinases (MAPKs)-including p38, ERK1 and ERK2 - in PCP-exposed lung and liver cells. Since NF-kB and MAPK signaling regulates the production of several inflammatory mediators, we determined the effect of PCP on cytokine/chemokine production. We observed a significant increase in the production of inflammatory mediators like: IL-1β, IL-8, CCL2, and CCL5 in PCP-challenged A549 and HepG2 cells. Additionally, we observed a substantial increase in the mRNA expression of; a) inflammation markers (IL-1β and IL-18), and b) master cytokines (IL-17A and IL-17F) in PCP-challenged cells. Overall, our results demonstrate a dysregulation in ROS generation and inflammatory responses in PCP-challenge in both human liver and lung epithelial cells.

55 Computational Modeling of Blood Metabolomics Biomarkers Addressing Racial Disparity

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Alcohol use disorders are among the most devastating disorders contributing to the global burden of disease (139 million disability-adjusted life-years). In the United States, over 8% of the population meets the criteria for alcohol dependence with alcohol-related problem cost exceeding 223 billion dollars, 88,000 deaths, and nearly 10,000 driving fatalities per year. Furthermore, alcohol contributes to over 200 diseases such as alcohol dependence, liver cirrhosis, cancers, and injuries. The FDA approved Acamprosate in 2004 to treat alcoholism (anti-craving drug). Multiple clinical trials have demonstrated that Acamprosate is effective in the maintenance of abstinence from alcohol in identified populations of alcohol-dependent individuals. A meta-analysis of 17 studies, which included 4087 individuals, showed continuous abstinence rates to be significantly higher in Acamprosate-treated subjects when compared to placebo. In this meta-analysis, the continuous abstinence rate after 6 months of Acamprosate treatment was 36.1%, which was significantly greater than the placebo rate of 23.4%. Given the variable efficacy of Acamprosate, the identification of biomarkers or genetic factors that could help predict treatment outcomes would represent a major public health benefit. We hypothesize that a metabolite in the blood of alcohol dependent patients could associate with anxiety based heavy drinking patterns and/or race, which may play an important role in explaining Acamprosate efficacy in subpopulations of alcohol dependent patients. In this proposal, we will develop biomarker paradigms to be applied to metabolomics and clinical measurement data using computational modeling. The results will allow us to establish a prediction algorithm between drinking patterns and depression in Acamprosate efficacy. Additionally, we will test whether racial disparity between Caucasian and African-American alcohol dependent populations influences the drinking pattern. The results from this study will suggest a prediction paradigm for the identification of a sub-population in alcohol dependence.

56 **Effect of Heat Shock Protein 90 Inhibition in Human Lung Microvascular Endothelial Cells**

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University of Louisiana at Monroe

The inhibition of the heat shock protein 90 (Hsp90) has been associated with both anti-inflammatory and anti-cancer effects. The endothelial barrier integrity, a crucial element of normal respiratory function, benefits from Hsp90 inhibition. In the current study we used human lung microvascular endothelial cells in order to investigate the effects of three different Hsp90 inhibitors (17-AAG, 17-DMAG and AUY-922) in the activation of the unfolded protein response (UPR) element. The Hsp90 inhibitors activated the UPR branches: Protein kinase RNA-like ER kinase, activating transcription factor 6, and inositol-requiring enzyme-1α. The expression of the UPR markers such as binding immunoglobulin protein, C/EBP homologous protein, endoplasmic reticulum oxidoreductin-1alpha, and protein disulfide isomerase, were also induced after treatment with those inhibitors. The results indicate that those compounds exert the potential to activate UPR, providing new information of the protective action of this class of compounds in the human vasculature. Future studies may investigate the exacts molecular pathways involved in the protective activity of Hsp90 inhibitors in the lungs, and contribute to the possible development of novel therapeutic strategy to enhance the weakened lung endothelial integrity due to inflammation. This study was supported by 1) The Institutional Development Award (IDeA) from the National Institute of General Medical Sciences of the National Institutes of Health (5 P20 GM103424-15 and 3 P20 GM103424-15S1) and 2) The R&D, Research Competitiveness Subprogram (RCS) of the Louisiana Board of Regents through the Board of Regents Support Fund (LEQSF(2019-22)-RD-A-26) to NB (PI).

57 **Expression levels of Mediator kinase module subunits and their interaction with transcription factors in mouse adipose tissue**

Ms. Sree Venigalla, Jamie Newman, Jacqueline Stephens
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Obesity is currently a major epidemic with obesity-related metabolic disorders such as type 2 diabetes, liver disease, and heart disease becoming more common. Dysregulation of genes associated with glucose and/or lipid metabolism is common in obesity-related disorders. Understanding how transcription factors and their cofactors regulate glucose/lipid metabolism has been a focus of many studies. Mediator is a large evolutionarily conserved transcriptional coactivator that directly binds to gene-specific transcription factors and RNA Pol II. The kinase domain, a dissociable four subunit module of the Mediator complex is made of subunits MED13, MED12, CDK8, and CCNC, that controls the expression of different subsets of genes to direct cell fate. Recent studies have shown that the kinase module is dissociated and degraded under feeding-induced activation of nutrient signaling in mouse livers. However, the downregulation of kinase module proteins in adipose tissue was not examined. This study determines the expression of protein levels of the kinase module

subunits between fasting and feeding in mouse adipose tissue depots where the expression of kinase subunits appears to remain constant in all adipose tissues when mice are fasted. However, following feeding the protein levels of subunits of the kinase module are decreased in most white adipose tissues except for mesenteric white adipose tissue (mWAT) and brown adipose tissue (BAT). Immunoprecipitation data provides evidence that MED12 and CDK8 interact differentially with transcription factors including STAT5A, CREBPa, PPARg, and SREBP-1c in preadipocytes and mature adipocytes. Future work will identify molecular details concerning the mechanism through which the Mediator is involved in the regulation of metabolism under physiological and pathophysiological conditions. Understanding these molecular mechanisms aids in identifying novel therapeutic targets for the treatment of metabolic disorders.

58 Multicolor carbon dots for Biology Imaging

Dr. Hua Wang, William Yu
Louisiana State University Shreveport

Carbon dots have attracted much attention as a new class of biocompatible nanomaterials due to their low toxicity, easy synthesis and excellent photostability. Here, we synthesized a new type of CDs which emit different color lights when they are in different environments. Moreover, the potential of our CDs for tumor cell imaging was studied with human head and neck squamous carcinoma cells. The experiment results indicated that our CDs were non-toxic to the target cells with a wide concentration range and the cells were successfully imagined on fluorescent microscope. The fluorescence emission of our CDs is more stable than that of commercial organic dyes which are widely used in cell tracking.

59 Folate receptor targeted release of Anti-inflammatory peptide from reducible thermosensitive nano-particles for treatment of Inflammatory diseases

Ms. Yaswanthi Yanamadala, Scott Poh
Louisiana Tech University

Immune cells like pro-inflammatory folate receptor-activated macrophages play a key role in the development of Inflammatory diseases. Most inflammation pathology treatments are encumbered by unwanted side effects that arise from the deposition of drug in unwanted tissues. The logical remedy for these undesirable properties involves selective targeting of the therapeutic agent to pathologic cells, thereby avoiding collateral toxicity to healthy cells. Previous work has demonstrated that activated macrophages overexpress folate receptors, but not resting macrophages. This property can be exploited for selective targeting and internalization of small molecular folate conjugates. However, little work has been done on nanoscale drug delivery systems such as biopolymer particle. Although peptide drugs may be effective in promoting anti-inflammatory effects, poor bioavailability limits its application. Hence, alternative delivery approaches must be sought. Temperature-sensitive polymeric nanoparticles (pNIPAM) have attracted much attention for their potential biomedical applications in delivering drug to tumor sites and inflamed tissues. For this study, we

designed a biocompatible polymer pNIPAM, a drug carrier for selective targeting and to protect the drug from enzymatic degradation. To improve the bioavailability of the drug we synthesized cell-penetrating peptides (CPP). Anti-inflammatory peptide (AIP) along with its CPP versions are synthesized, characterized, and introduced into folate-conjugated fluorescein-pNIPAM. RAW macrophage cells are incubated with AIP, CPP, and peptides internalized nanoparticles and imaged using a fluorescence imaging microscope. CPP incubated cells showed better cell penetration compared to normal AIP. Further investigation to compare the uptake of targeted and nontargeted folate receptor treatment must be done to analyze whether the uptake is folate-receptor mediated.

60 **Tumor Grade, Patient Age and Geographical Area Related Racial Disparity Patterns in Prostate Cancer Mortality: Epidemiological Implications and the Underlying Molecular Biology**

Dr. Kun Zhang, Wensheng Zhang, Yan Dong, Oliver Sartor, Erik K. Flemington
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A major racial disparity in prostate cancer (PCa) is that African American (AA) patients have a higher mortality rate than European American (EA) patients. We filtered the SEER 2009-2011 records and divided them into four groups regarding patient race and cancer grades. On such a partition, we performed a series of statistical analyses to further clarify the aforementioned disparity. Molecular evidence for a primary result of the epidemiological analysis was obtained from gene expression data. The results include: (1) Based on the registry-specific measures, a significant linear regression of total mortality rate on the percentage of high-grade cancers (PHG) is demonstrated in EAs ($p < 0.01$) but not in AAs; (2) PHG and its racial disparity are differentiated across ages and the groups defined by patient outcomes; (3) For patients with cancers in the same grade category, i.e. the high or low grade, the survival stratification between races is not significant in most geographical areas; and (4) The genes differentially expressed between AAs' and EAs' tumors of the same grade category are relatively rare. The perception that prostate tumors are more lethal in AAs than in EAs is convincing regarding AAs' higher PHG. However, this perception is questionable when the comparison is focused on cases within the same grade category. Supporting observations for this conclusion hold a remarkable implication for erasing racial disparity in PCa. That is, 'Equal grade, equal outcomes' is not only a verifiable hypothesis but also an achievable public health goal.

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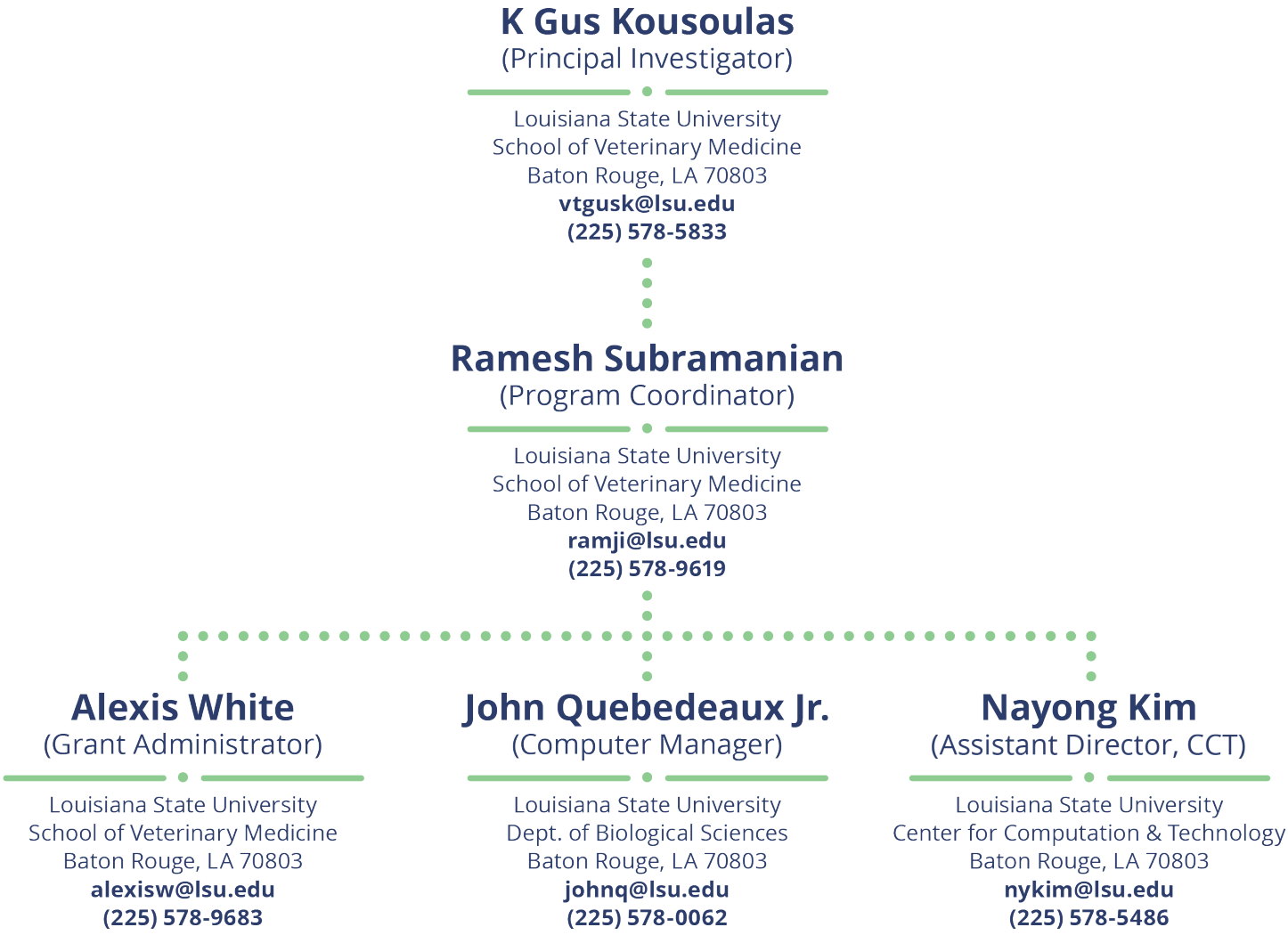
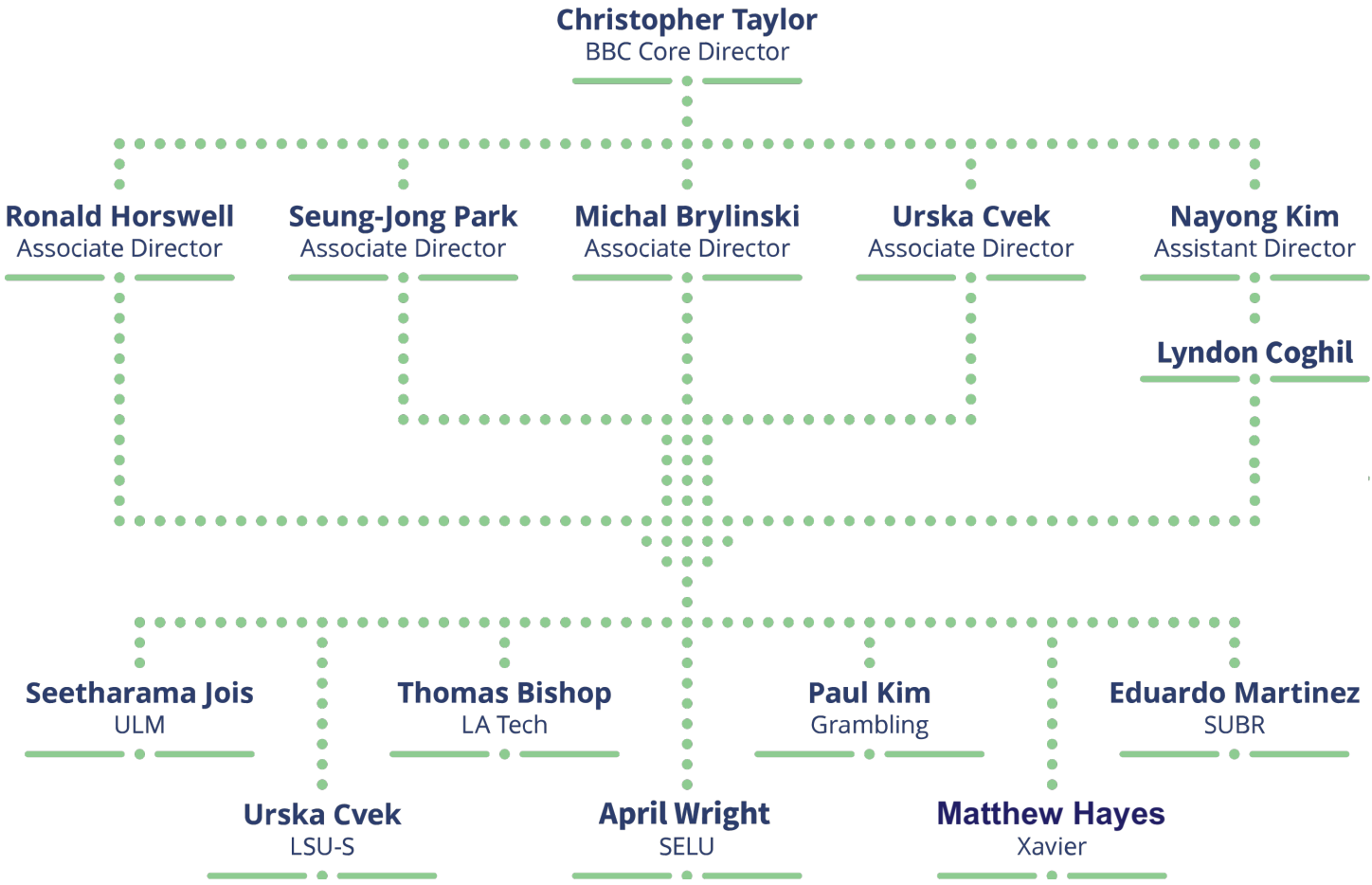
Administrative Core



Core Structures and Committees

Bioinformatics, Biostatistics, and Computational Core



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May 25 - July 31, 2020	Summer Undergraduate Research Program