Arkansas INBRE Research Conference

Arkansas IDeA Network of Biomedical Research Excellence

Schedule of Events

Friday, October 21, 2016

12:00 p.m. to 1:30 p.m.	Registration (Chancellor Hotel Atrium, 2 nd floor). Graduate
	Program Information available from 12:00-1:30.
1:30 p.m.	Opening Session, chaired by Professor Ralph Henry,
	Biological Sciences, University of Arkansas.
	(Chancellor Hotel, Eureka Springs Ballroom)
1:35 p.m. to 3:00 p.m.	Invited faculty presentations
3:00 p.m. to 3:15 p.m.	Set-up time for student orals
3:00 p.m.	Official hotel check-in
3:15 p.m. to 5:00 p.m.	Undergraduate oral presentations (Chancellor Hotel, Biology -
	Eureka Springs Ballroom ABC; Chemistry – Bella Vista Room;
	Physics - Eureka Springs Ballroom D). (12 minute talks with 3
	minutes for questions)
5:15 p.m. to 6:15 p.m.	Faculty Discussion Group and Reception
	(Chancellor Hotel, Lounge and Restaurant, First Floor)
5:15 p.m. to 6:15 p.m.	Student Discussion Group and Reception
	(Chancellor Hotel, Atrium)
6:30 p.m.	Banquet (Fayetteville Town Center)
7:15 p.m.	Featured Speaker Dr. Steven Harms, M.D.
Saturday, October 22, 2016	5
7:30 a.m. to 8:00 a.m.	Poster Set-up begins (Hillside Auditorium, Physics Building)
7:30 a.m. to 10:00 a.m.	Conference Registration (Upper Hillside Lobby)
7:45 a.m. to 9:30 a.m.	Continental breakfast (Upper Hillside Lobby, Physics Bldg.)
7:45 a.m.	Poster judges receive assignments (Hillside Auditorium for
	Biology and Chemistry, Physics Building for Physics judges)
8:00 a.m. to 9:00 a.m.	Poster Session A (Hillside and Physics)
9:00 a.m. to 9:15 a.m.	BREAK – Remove Session A posters (except Physics).
	Put up Session B posters.
9:15 a.m. to 10:15 a.m.	Poster Session B (Hillside and Physics)
10:30 a.m. to 11:45 a.m.	Workshops and Tours (UA Campus, various locations)
11:55 a.m.	Award presentations & conclusion, Hillside Auditorium 202

Registration Information

The INBRE registration desk will be open:

- Friday 12:00 p.m. to 5:00 p.m., Chancellor Hotel Atrium (2nd floor)
- Saturday 7:30 to 10:00 a.m., Hillside Auditorium, Upper Lobby

Travel Subsidies are no longer being given.

Lodging will be at the Chancellor Hotel, 70 N. East Avenue, Fayetteville, AR 72701. **Parking:** Friday parking is complimentary in the Municipal Parking Garage, third level only (first level card access for registered guests of the Chancellor Hotel). Parking in the parking garage behind the Town Center is free all day Friday and Friday night.

Saturday parking is free on the UA campus in designated yellow-sign lots and parking decks. Please see the map at end of program.

Arkansas INBRE

The Arkansas IDeA Network of Biomedical Research Excellence (Arkansas INBRE) is funded by a grant from the National Institute of General Medical Sciences (NIGMS), under the Institutional Development Award (IDeA) Program of the National Institutes of Health (NIH). The IDeA program was established for the purpose of broadening the geographic distribution of NIH funding for biomedical and behavioral research. Currently NIGMS supports INBRE programs in 23 states and Puerto Rico.

The Arkansas INBRE builds on the successful Arkansas Biomedical Research Infrastructure Network (BRIN) program that was established in 2001 under a grant from NCRR. The Arkansas BRIN established a statewide network that links Arkansas institutions of higher education to establish and maintain a statewide infrastructure in support of growing efforts to build capacity for biomedical research in Arkansas. http://brin.uarms.edu/default.asp

Arkansas INBRE Research Conference

The Arkansas INBRE Research Conference is sponsored by Arkansas INBRE and is hosted by the departments of biological sciences, physics, and chemistry and biochemistry, Fulbright College of Arts and Sciences, University of Arkansas.

Conference Planning Committee

Denise Greathouse, chemistry and biochemistry Ravi Barabote, biological sciences Leslie Johnson, chemistry and biochemistry Roger Koeppe, chemistry and biochemistry Reeta Vyas, physics

INBRE Steering Committee

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*****Staff***** Diane McKinstry, UAMS, Program Coordinator **Caroline Miller Robinson,** UAMS, Business Manager Linda Williams, UAMS, Research Liaison

Biotechnology Core Leaders Joshua Sakon, UAF Alan Tackett, UAMS

Poster Session and Awards

Display

Poster set-up begins at 7:30 a.m. Saturday in Hillside Auditorium, Lower Level, and Physics Building.

Session A - 8:00 a.m. to 9:00 a.m. 9:00-9:15 BREAK. Biology and Chemistry Posters: Take down Session A posters. Put up Session B posters. Session B - 9:15 a.m. to 10:15 a.m.

Presenters are expected to be present during the scheduled time. Business or business casual dress is encouraged. *See index and abstracts in this program for numbers and Session assignments.*

Awards

Prizes will be awarded to the top oral and poster presentations in the undergraduate category in each discipline. The awards will be presented Saturday at 11:55 a.m. in Hillside Auditorium Room 202. Presenters must be present at the awards presentation to receive an award.

Judging Rules

Each undergraduate oral presentation and poster will be judged by at least two judges, selected from various institutions. To avoid a possible conflict of interest, no judge will evaluate a presentation from his/her own institution.

Awards will be given in each of the three disciplines – physics, biology, and chemistry and biochemistry. Only oral/posters with undergraduate participation, and where the designated presenter is an undergraduate student, will qualify for awards.

Featured Speaker

The Technology Road for Breast MRI

Steven E. Harms, M.D.



Dr. Steven E. Harms, MD, FACR serves as Medical Director of Aurora Imaging Technology Inc. M.D. Degree from the University of Arkansas for Medical Sciences in 1978.

ABSTRACT: Magnetic resonance imaging (MRI) is conceptually different from any other imaging technique. Other methods are similar to light exposing a photograph where x-rays or sound waves are passed through the body and an image is created through differential absorption or reflection by the tissues. Paul Lauterbur first described MRI in 1973 where an image was made of two capillary tubes inside an NMR tube. Lauterbur's genius was in the use of magnetic field gradients to spatially encode the radio signals. The motivation for making MR images developed from the discovery in 1971 by Damadian that cancer could be distinguished from benign tissues on NMR by the prolongation of T1 (spin lattice)

relaxation times. Magnetic resonance is important for medical diagnosis because the signals tell a story about the molecular environment of the tissues.

Breast cancer is the most common malignancy and the second most common cause of cancer deaths in women. Early researchers recognized the potential for MRI to detect breast cancer. In fact, human breast cancers were imaged before the brain or spine (the most common current MRI applications). However, early clinical trials using breast MRI failed to show any improvement over mammographic (x-ray based) images. Subsequently, efforts to use MRI for breast cancer detection subsided.

When gadolinium contrast agents were introduced in Europe in the late 1980's, a German researcher, Warner Kaiser, used contrast-enhanced breast MRI to demonstrate breast cancers. However, the enhancing breast cancers were often obscured in the breast by fat because they have a similar T1. Encouraged by Kaiser's discovery, our laboratory at Baylor developed an efficient method for generating breast MR images where the fat is not excited. Cancers showed up like bright stars in a dark sky. This concept has been widely shown in clinical trials around the world to vastly improve the detection of breast cancer. When screening women for breast cancer, mammography detects about 4 cancers per 1000 screens. Breast MRI has about 10 times the cancer detection rate (40 per 1000).

Our current challenge is to improve the cost effectiveness of screening. MRI is expensive technology. We are currently participating in a NCI sponsored trial to test a streamlined breast MRI protocol that should reduce costs by improving scanning efficiency. This could cut imaging costs by 50% or lower. New technology called STEREO from the University of Minnesota is in development that could significantly lower the cost of the MRI system. This new technology could allow MRI equipment costs to be reduced enough to compete with x-ray machines in price. Another approach is to develop novel, low cost, non-imaging technology for more

frequent and widespread screening. A screening method was proposed by Suzanne Klimberg at UAMS to identify high-risk proteins in tears. This test would reduce costs by limiting imaging to selected high-risk patients instead of widespread screening.

Clinical trials using mammographic screening show a reduction in mortality that approaches 50%. Yet, mammography is only about 25% sensitive. It is likely that improved screening methods could provide an even greater reduction in mortality. The detection of smaller cancers provides the potential for less treatment at a lower cost.

Dr. Steven E. Harms is recognized nationally in the area of magnetic resonance imaging (MRI), specifically Breast MRI, and was named "Komen Foundation Scientist of the Year" by Susan G. Komen for the Cure in 1998. In 1995, he was given the annual William Beaumont Award by the American Medical Association for the outstanding physician in the nation under the age of 50. He was formerly on the faculty at the University of Arkansas for Medical Sciences (UAMS), Baylor University Medical Center, and M. D. Anderson Cancer Institute. During his 14 years as director of MRI at Baylor, Dr. Harms and his research team developed MRI applications including RODEO Breast MRI. He helped draft the 2007 American Cancer Society breast cancer screening guidelines that recommend breast MRI screening for high risk patients. He served as member and chairman of the Radiologic Devices Panel for the US Food and Drug Administration from 1983-2001. Harms is a fellow of the Society of Breast Imaging, a fellow of the American College of Radiology, and has been on the Best Doctor's in America since 2003. Harms practices at MANA's The Breast Center in Fayetteville, Arkansas since 2004 and continues to be a clinical professor at UAMS.

Dr. Harms has authored over 116 scientific papers, 43 book chapters, and 11 patents. He is past-president of the International Society of Magnetic Resonance in Medicine. Dr. Harms was previously on the board of directors and program chair for the American Society of Breast Disease and the Society of Magnetic Resonance in Medicine. Dr. Harms served on the American College of Radiology Breast MRI Lexicon Committee and the Susan G. Komen Public Policy Committee. He was previously associate editior of the Journal of Magnetic Resonance Imaging and The Breast Journal. He has been a visiting professor at medical schools throughout the world including Harvard, Johns Hopkins, Northwestern, Stanford, Yale, Peking Medical University, Taipei Medical University, and University College London.

Participating Institutions

Arkansas State University Arkansas Tech University Central Baptist College Harding University Henderson State University Hendrix College Heyoka Technical Consulting John Brown University Lyon College **Missouri State University** Northeastern State University Northwest Arkansas Community College **Ouachita Baptist University** Philander Smith University **Pittsburg State University Rhodes** College Southern Arkansas University **Truman State University** University of Arkansas at Fayetteville University of Arkansas at Fort Smith University of Arkansas at Little Rock University of Arkansas at Monticello University of Arkansas for Medical Sciences University of Arkansas at Pine Bluff University of Central Arkansas University of Missouri University of the Ozarks Williams Baptist College

Invited Faculty Presentations

Friday from 1:30 p.m. to 3:00 p.m. (Chancellor Hotel, Eureka Springs Ballroom ABC)

No registration required



Dr. Melissa Kelley, Ph.D.

Professor, Department of Chemistry University of Central Arkansas (1:35 – 2:00)

TITLE: Wisdom from a Fortune

Cookie: Retinoid Regulation of Cellular Adhesion and Proliferation in K562 Cells

Abstract: Establishment and maintenance of proper immunity requires a precise balance between cellular adhesion and proliferation. A disruption in either event results in a variety of pathologies encompassing immunosuppression, auto immunity, and cancer. Vitamin A (retinol) and its analogs, retinoids, profoundly affect immune function by mediating cellular adhesion and proliferation. The interplay between cellular adhesion and proliferation is complex; however, integrins, particularly the α 5 β 1 subset, play a pivotal role in orchestrating critical cellular signals that culminate in cellular adhesion and growth. Retinoids modify the expression of a variety of adhesive/proliferative signaling proteins including, $\alpha 5\beta 1$ integrins; however, the role of specific retinoic acid receptors involved in these processes has not been elucidated. Our laboratory is taking the first steps into delineating the mechanism of how retinoid receptors differentially regulate cellular adhesion and proliferation through modulation of integrins. In this talk, I will describe our work, which focuses on the effect of all-



surface expression.

trans-retinoic acid receptor (RAR)

agonists on K562 cellular adhesion, proliferation, and α 5 β 1 integrin cell

Dr. Bret Lehmer,

Ph.D.

Assistant Professor Department of Physics University of Arkansas (2:05 – 2:30)

TITLE: Putting into Context

Gravitational Wave Sources: The Link to X-ray Binary Populations

Abstract: The recent detection of gravitational waves by LIGO has generated enormous excitement, as an entirely new and powerful means for studying the Universe has opened. The gravitationalwave emitting binary stars that have been detected, and will continue to be detected by LIGO (and other near-term gravitational-wave detectors) represent a merging phase of two compact stellar remnants: combinations of black holes and neutron stars. Prior to such a merger phase, these systems would have inevitably evolved through an X-ray binary phase, in which the more massive compact object would have accreted from its not-yet-evolved companion star and produced bright X-ray emission. In this talk, I will describe my research on X-ray binary star populations throughout the Universe. I will place into context the gravitational-wave emitting binary populations that will be observed in the coming years, and will highlight what these sources tell us about the Universe. Finally, I will highlight some exciting future observatories that will provide new information about these sources.



Dr. Tsunemi Yamashita, Ph.D.

Professor of Biology Arkansas Tech University (2:35 – 3:00)

TITLE: Characterization of

Genes and Toxins from a Scorpion that Possesses a Mild Venom

Abstract: Venomous animals have long fascinated and terrified humans. Among them, scorpions have been noted for their medically important venom. All scorpions are venomous, yet only the Buthid family is seen as markedly harmful to humans. Within the Buthids, some species are known to significantly affect humans, yet other species do not. Much of the previous work has focused upon venom toxin proteins in known medically relevant species, with little attention to those scorpion species possessing mild venom. Scorpion species with mild venom may house components amenable for medical research. In our current research work, we investigate and characterize sodium channel toxin proteins in C. vittatus, a species in the medically important genus, Centruriodes. We have outlined our research activities with the following objectives. First, to investigate the variability and organization of sodium toxin genes we will sequence, assembly, and annotate its genome. Second, gene expression studies on specific sodium toxin genes will be conducted to determine differential expression in these genes. Third, two sodium toxin proteins will be overexpressed to create pure sodium toxin protein to determine if structural and functional differences exist in C. vittatus sodium toxin protein compared to other Centruroides species. In this presentation, I will further describe our approach and discuss the current results obtained through this research project.

3:00 p.m. - Announcement of NIH IDeA National Resource for Proteomics

Dr. Alan Tackett, Ph.D.

Professor of Biochemistry & Molecular Biology, Pediatrics and Pathology University of Arkansas for Medical Sciences

Student Oral Presentations

Undergraduates will give 12-minute oral presentations from 3:15 p.m. to 5:00 p.m. on Friday. All talks will take place at the Chancellor Hotel. Students were chosen based on abstracts and willingness to present an oral platform talk. Additional information, authors, and footnotes can be found in the complete list of abstracts in this program.

Biology Oral Presentations

(Eureka Springs Ballroom ABC) Michael Ceballos, Chair

Brianna LaFerney, Harding University

(3:20 p.m.) Proliferation in Human Bronchial Epithelial Cells Following Exposure to Carbon Black and Protection of Heat Shock Pretreatment Lindsey Wood, Southern Arkansas

University

(3:35 p.m.) Identification of Novel Variant of Cannabinoid Receptor CB1 in Cancer Cells Continuation

Dylan Gilbreath, Hendrix College

(3:50 p.m.) Development of the mouse vomeronasal organ in the absence of Dlk-1 gene function

Gina Hauptman, University of Arkansas

(4:05 p.m.) Transcriptional regulation of robo2 in the Drosophila embryonic nervous system

Anna Sharabura, Hendrix College

(4:20 p.m.) Collagen Increases Tumorigenicity of Papillary Thyroid Cancer Cells Harboring BRAFV600E Mutations

Garrett Koehn, Harding University

(4:35 p.m.) SLCO1B1 Genetic Polymorphisms are Potentially Linked to Blood Pressure and Triglyceride Levels in a Postmenopausal Female Cohort

Chemistry and Biochemistry Oral

Presentations (Bella Vista Room) Jingyi Chen, Chair

William Staton, Lyon College

(3:20 p.m.) Utilizing a Mutated Taxus Benzoyltransferase (mTBT) as a Biocatalyst Nicholas S. Kowalkowski, Ouachita Baptist University

(3:35 p.m.) The Effect of Glutamine and y-Glutamylglutamine on NIH-3T3 Cell Metabolism

Tia'Asia James, University of Arkansas at Pine Bluff

(3:50 p.m.) Synthesis and Analytsis of Superparamagnetic Bridged Lanthanide (III) Complexes

Amanda Paz Herrera, University of the Ozarks

(4:05 p.m.) Detection of Helix Fraying in Transmembrane Helices with Interfacial Histidine Residues

Danica Ordonez, University of Central Arkansas

(4:20 p.m.) Conformational Protein Ensemble of the Calmodulin Ligand PEP-19

Madison Perchik, Rhodes College

(4:35 p.m.) DFT Study of the Selectivity of Phenylalanine Hydroxylase (PheOH)

Physics Oral Presentations

(Eureka Springs Ballroom D) Hugh Churchill, Chair

Orion Guan, Truman State University

(3:20 p.m.) Photoelectrical
Characterization of Bacteriorhodopsin
suspended in a lipid bilayer membrane
Luke Fairbanks, Rhodes College
(3:35 p.m.) Ultrasonic Bone Assessment
using Backscatter Power Difference
Technique

Joseph Matson, Hendrix College

(3:50 p.m.) Anisotropic Differential Reflectance Spectroscopy of Thin GeSe **Taylor Burdick, Southern Arkansas University**

(4:05 p.m.) Suppression of Radiation-Induced Chromosome Damage by GT3 and the Role of Microgravity

Jesse Underwood, Missouri State University

(4:20 p.m.) Molecular Dynamics Simulations of the Mechanical and Structural Properities of Silica and Aluminosilica Mesoporous Materials Jacob Russell, John Brown University (4:35 p.m.) The Indeterminate Case of Classical Static Friction when Coupled with Tension

Saturday Workshops

INBRE participants are expected to attend a workshop as part of the program. All workshops and tours will take place Saturday at <u>10:30</u> a.m., in various locations on the University of Arkansas Campus

Registration for Workshops will be at Conference Registration Table

Workshop 1 - Career Workshop, Skills and Expectations Required to Succeed in Today's Job Market

(Chemistry Building, Room 132) Denise Greathouse, PhD, UAF This workshop is targeted to undergraduate students as they prepare to enter the job market. In the first part of the workshop a short presentation, Critical Skills in a Rapidly Changing World, will highlight some of the important skills employers are seeking in today's job market. The second part of the workshop will be comprised of a panel of University of Arkansas graduates who are now working at 'start-up' companies in Arkansas. After a brief introduction, students will have the opportunity to ask the panelists questions about career choices, education expectations, typical daily tasks, skills and gualifications, etc. Panelists:

<u>Anna Daily</u>, Ascendant Dx, Chief Scientist <u>Kevin Schoelz</u>, Picasolar Inc., Research Scientist; Arkansas Tech, Visiting Profesor <u>Mike Rutherford</u>, Chief Scientist, TiFiber, Inc.

Workshop 2 - Nanochemistry

(Chemistry Building, Room 144) **Jingyi Chen, PhD**, UAF Limited to 15 participants

Nanochemistry plays an important role in many applications ranging from medicines to catalysis, electronics, energy conversion and storage. In this workshop, the emphasis is the nanochemistry in theranostics applications, in particular, the use of nanoparticles in disease diagnostics and therapy. An overview of nanomedicine will be presented, followed by a specific example based on the gold nanostructure nanoplatform.

Workshop 3 - Molecular Modeling

(Chemistry Building, Room 308) **Peter Pulay, PhD**, Dept of Chemistry and Biochemistry

Limited to 12 participants or groups. If feasible, bring a computer, although this is optional.

Methods of molecular modeling on a personal computer will be addressed, with software available for distribution to up to 12 individuals or cluster teams.

Workshop 4 – STEAM-H: Collaborate, Innovate, and Inspire

your Community (Nano Atrium) Shilpa Iyer, PhD, Biology Department. Limited to 30 participants. This workshop will engage participants in the power of integrative STEAM-H (Science, Technology, Engineering, Arts, Mathematics, Health) approaches to communicate significant public health concerns related to mitochondrial and obesity-related disorders.

Workshop 5 - Cellular Mechanisms of Salt and Water Transport in Fish

(Ferritor Building, Room 317) Christian Tipsmark, PhD, Professor of Biology, UAF

The goal of physiological research is to understand the function of living systems from the level of the whole organism and its organs to that of the single cells and bio-molecules. This workshop highlights mechanisms and regulation of salt and water transport in fish and demonstrates some of the methods used in physiology. It will cover experimentations with whole animals and isolated tissues. Tehcniques demonstrated will include enzyme assays, specific mRNA and protein quantification and cellular localization of specific proteins with immunofluorescence.

Workshop 6 - Machine Learning for Bioinformatics

(Gearhart Hall (formerly Ozark Hall), Room 101 computer lab) Philip Hudson Williams, PhD, **Bioinformatics Tech Director, UALR** Limited to 30 participants. Some bioinformatics solutions involve predictors and classifiers. Machine Learning is a method to train accurate predictors and classifiers. This workshop demonstrates C5.0, a decision tree method for training a predictive model. Different data types are used as examples in training. Validation methods are introduced. Using a trained model for prediction of unknown cases is demonstrated.

Workshop 7 – Physics: "A 2D How-to"

(Physics Building, Room 134) Hugh Churchill, PhD, Professor of Physics, UAF

Limited to 15 participants.

After a brief introduction to the field of 2D material research, I will demonstrate the now-famous "Scotch tape technique" that is used to peel apart atomically thin layers of graphene and many other 2D materials from 3D crystals. Workshop attendees will then have the opportunity to try this themselves using tape, tweezers, and silicon chips, followed by "flake hunting" with a microscope.

Workshop 8 - Single-Molecule Localization Microscopy

(Physics Building, Room 133 and Room 115A)

Yong Wang, PhD, Professor of Physics, UAF

Limited to 15 participants

This workshop will briefly introduce the basics of single-molecule localization microscopy, which improves the resolution of light microscopy from 200 nanometers to 10 nanometers. Attendees will have a chance to perform hands-on experiments to localize single fluorescent particles with a precision of several nanometers and track the diffusion of single particles.

Workshop 9 - Relawavity: Simple Trigonometry Leads to Understanding of Relativity and Quantum Theory

(Physics Building, Room 241) William Harter, PhD, Professor of Physics, UAF; T.C. Reimer, PhD, (Heyoka Co.); AI Calabrese, UAF Modern science from astrophysics to zoology depends increasingly on two pillars of modern physics, special relativity (SR) and quantum mechanics (QM), that are based on properties of light waves. The bioscience renaissance could not happen without the optics of maser, laser, UV, X0ray, and synchrotron effects due to SR and QM theory that is still regarded as esoteric mystery. This workshop seeks to demystify SR and QM theory using high school trigonometry of plane light waves. Using diagrams of circle trig functions (sin σ , cos σ , tan σ) and

inverses (csco, seco, coto) we show that each one is also a hyperbolic function that is key to SR and QM.

INBRE 2016 - Nano Building Tour (Nano Building Room 105) Professor Greg Salamo and graduate student Tim Morgan

Students will have the opportunity to visit Nano Building facilities, learn about nanoscience and get hands-on experience on how to image a sample with nanoscale resolution using a scanning electron microscope (SEM).

INBRE 2016 - Physics Lab Tours

Nano-Optics Lab:

Joseph Herzog, (PHYS 245) In the Nano-optics lab, students measure the optical properties of nanostructures both with computer simulations and an advanced, custom optical microscope and spectroscopic setup. In the computer models, students work on designing nanostructures with optimal optical properties. The experimental optical setup characterizes the optical properties of the nanostructures with dark-field spectroscopy, photo-luminescence, bright-field imaging, and Raman spectroscopy. Most of the nanostructures that are investigated are plasmonic structures. These structures can enhance and focus light at the nanoscale, below the diffraction limit of light. Other studies in the lab investigate the light interactions in biological structures and photonic crystals. Photonic crystals are nanoscale structures which can reflect, guide, and bend light very efficiently. Additionally, students in the Nano-Optics lab use other labs around campus to fabricate the optical nanostructures.

Laser Physics/Quantum Optics Lab:

Surendra Singh, (PHYS 128/130)

Investigations of polarization and phase properties of optical beams, optical vortices, statistical and dynamical properties of light generated in lasers and nonlinear optical systems, and light scattering studies of bio-molecules are being carried out.

Abstracts

Presentations are <u>posters</u>, on Saturday, unless denoted as "<u>**Oral**</u>" for Friday afternoon.

Biological Sciences

Friday Oral Platform Session

ORAL – 3:20. Proliferation in Human Bronchial Epithelial Cells Following Exposure to Carbon Black and Protection of Heat Shock Pretreatment. Brianna LaFerney. Department of Biology, Harding University, Searcy, AR 72143

The increasing introduction of nanomaterial use into industry, technology, and medicine calls for a higher understanding of the physiological and cellular effects of nanoparticle exposure. Carbon Black (CB) is a 80-130 nm material composed almost entirely of elemental carbon that may be suspended in air as particulate matter air pollution. This nanoparticle is known to cause adverse effects to the environment and to human health following inhalation, yet its cellular effects remain largely undefined. Previous research has shown the endocytosis of CB particles into the cell and induction of mitochondrial stress leading to apoptosis, a form of programmed cell death. The aim of research was to characterize effects of cytotoxic CB on proliferation of human bronchial epithelial cells (16HBE14o- cells), as well as assess the efficacy of heat shock (HS) pretreatment to protect cells from CB-induced apoptosis. It was hypothesized that both acute high dose and chronic low dose CB exposure would be sufficient to reduce levels of cellular division and that upregulation of heat shock proteins (Hsp) by HS pretreatment would lend protection against proapoptotic factors induced by CB. HS treatment at 45°C resulted in higher Hsp expression than HS treatment at 42°C, yet the higher temperature left the cells more susceptible to CB cytotoxicity, while the lower temperature exhibited cellular protection. Acute CB exposure reduced levels of cellular division while chronic CB exposure increasingly reduced quantity of viable cells as exposure time progressed over the course of one month. Acquiring more extensive knowledge of carbon black's physiological and cellular effects is a vital step towards discovering treatment and a more full understanding of the nature of nanoparticles.

ORAL – 3:35. Identification of Novel Variant of Cannabinoid Receptor CB1 in Cancer Cells

Continuation. <u>Lindsey Wood</u>, Dr. Anna Radominska-Pandya, Azure Yarbrough, Sebastian Pyrek. *Department* of Molecular Biology and Biochemistry, Southern Arkansas University, Magnolia, AR 71753.

Cannabinoids receptors (CBRs) are G-protein coupled receptors (GPCRs) activated by the binding of a cannabinoid ligands. The two classic cannabinoid receptors are CB1 and CB2. It was recently shown that CB1, which is mostly expressed in the brain, and CB2, mostly expressed in the spleen, have been found to be overexpressed in different cancers models. However, no information is available on the expression CB1 variants in cancer. My previous preliminary experiments, using semi-quantitive reverse transcription polymerase chain reaction (RTPCR) and primers corresponding to the brain variants of CB1, demonstrated that in several cancer lines, varying sets of CB1 with differing sizes were expressed. Specifically, we had shown that brain, pancreatic, and breast cancer cell lines expressed different size constructs. High inter-cancer variations were observed; some cancer lines did not have any constructs, others have expressed brain-style variants, or variants with different length. Based on these prior experiments, we hypothesize that the cancer cells under investigation, express variants identical to those observed in brain, but can also express different, cancer-specific CB1 variants. Our current strategy is to identify the PCR products of different variants by sequencing, cloning, and eventually expression in the cell lines. If the project is successful, the physiological significance of these splice variants can be understood, and it is feasible that the cancer-specific variants could potentially be targets of cannabinoid anti-cancer drugs.

ORAL – 3:50. Development of the mouse vomeronasal organ in the absence of Dlk-1 gene function. <u>Dylan</u> <u>Gilbreath</u>, Rebecca Seal, Alan Umfress and Richard Murray. Department of Neuroscience, Hendrix College, Conway, AR 72032.

In mice, the vomeronasal organ (VNO) is a small, cigarshaped organ located on either side of the nasal septum just above the roof of the mouth. The VNO is connected to the nasal cavity and contains sensory neurons that detect inhaled pheromones. The sensory neurons of the VNO are derived from the olfactory placode which forms on the surface of the embryo and invaginates to form the nasal cavity. The VNO proper separates from the rest of the nasal cavity beginning around embryonic day (E) 10.5 when it invaginates toward the nasal septum. Little is known about the genetic regulation of the invagination process or the specification of neural stem cells in this organ. Preliminary work in our lab found that the Dlk-1 gene is expressed in a ventral subset of cells in the developing VNO at E10.5. This pattern of expression suggests that it may be involved in either the invagination of the epithelium or the specification of neural stem cells during VNO development. To determine if the Dlk-1 gene is required

for the normal development of the VNO, we obtained mice that contain a null allele of the Dlk-1 gene and examined the development of the VNO in Dlk-1 knockouts. We have found that the VNO invaginates properly in the absence of Dlk-1 function in the knockout embryos, but the development of VNO sensory neurons may be altered. We are currently characterizing the expression of cell type specific markers in embryonic and postnatal animals to determine if Dlk-1 is required for the development of vomeronasal sensory neurons. Supported by the Arkansas INBRE program and the Hendrix Odyssey Program.

ORAL – 4:05. Transcriptional regulation of robo2 in the **Drosophila embryonic nervous system.** <u>Gina Hauptman</u> and Tim Evans. *Department of Biological Sciences, University of Arkansas, Fayetteville, AR* 72701.

During nervous system development, neuronal axons are guided to their synaptic targets by receptors expressed on the surface of the axon. The Drosophila Robo2 axon guidance receptor is a member of the evolutionarily conserved Roundabout (Robo) protein family, and controls a number of axon guidance decisions during embryonic development. For example, Robo2 regulates midline crossing of axons in response to the repellent ligand Slit, and specifies the mediallateral position of longitudinal axon pathways in the ventral nerve cord. The different roles of Robo2 depend on its expression in various subsets of cells within the central nervous system (CNS). Thus, precise regulation of Robo2 expression is an important aspect of nervous system development in Drosophila. To investigate the genetic regulation of Robo2 expression, we looked for regulatory elements in and around the robo2 gene. We screened seventeen Janelia GAL4 lines to find those that reproduced aspects of Robo2's expression pattern in the CNS. Our observations indicate that different aspects of Robo2 expression are conferred by distinct regulatory elements in the robo2 gene. Specifically, we identified fragment GMR28F02 as a potential regulatory element in the development of longitudinal axons in the CNS and fragment GMR28E07 as a potential regulatory element controlling Robo2 expression in midline glial cells. To determine the relationship between transcriptional regulation of robo2 and its various functional roles in axon guidance, we generated a robo2 rescue construct in which each of the putative regulatory regions is used to drive expression of an HA-tagged robo2 cDNA. We will compare HA expression in these transgenic lines to endogenous Robo2 expression, and perform rescue experiments with a robo2 mutant background to assay the ability of each fragment to restore Robo2 function in various axon guidance contexts.

ORAL – 4:20. Collagen Increases Tumorigenicity of Papillary Thyroid Cancer Cells Harboring BRAFV600E

Mutations. <u>Anna Sharabura</u>, LeeAnn Jolly, Aime T. Franco, Laura J. MacDonald. *Biology Department, Hendrix College, Conway, AR* 72032.

Thyroid cancer is the most common endocrine cancer, and incidence is increasing worldwide. Thyroid cancer can be classified as either well-differentiated or poorly differentiated. Of well-differentiated thyroid cancers, papillary and follicular thyroid cancers are most common, but are associated with different genetic mutations and display different pathologies and sites of metastasis. Activating BRAF mutations are prevalent in papillary carcinoma, which metastasizes to lymph nodes in the neck, while activating HRAS mutations are most prevalent in follicular carcinoma, which metastasizes to the lungs and bones. While our understanding of the genetic basis for thyroid cancer continues to expand, less is known about how the tumor microenvironment alters tumorigenic characteristics of thyroid tumor cells. Recently, Jolly et al. reported that papillary thyroid tumors derived from cells harboring activating BRAFV600E mutations and PTEN deletions are enriched with fibrillar collagen which is associated with decreased survival. In this study, we investigated whether growth on collagen enhanced tumorigenic characteristics of papillary thyroid cancer cell lines with BRAFV600E mutations. Three distinct cell lines were grown on collagen and assessed for morphology, proliferation, altered activation of signaling pathways, and cellular secretion or reception events. Interestingly, our results suggest that growth on collagen increases small vesicle secretion by tumor cells, which may be important for signaling required for metastasis. These and other results implicate an important role for collagen in the progression of thyroid cancer.

ORAL – 4:35. SLCO1B1 Genetic Polymorphisms are Potentially Linked to Blood Pressure and Triglyceride Levels in a Postmenopausal Female Cohort. <u>Garrett S.</u> <u>Koehn</u>, Brandi L. Clark, Daniel H. Atchley, Michael A. Murphy, and Landry K. Kamdem. *College of Pharmacy, Harding University, Searcy, AR* 72143.

Background: Since SLCO1B1 Genetic Polymorphisms have been found to be linked to essential hypertension1, enalapril-induced cough2, and statininduced myopathy3, we hypothesize that SLCO1B1 genetics could also play a role in the physiology of blood pressure and lipid homeostasis.1 To test the hypothesis that SLCO1B1 impacts blood pressure and lipid values, postmenopausal females' SLCO1B1 genetics were found and statistically analyzed by the genotypes' relations to subjects' blood pressure and lipid levels. Methods: DNA of postmenopausal females (n=84) was used in this investigation. The SLCO1B1 SNPs of interest were genotyped by UAMS Genomics Core (Dr. Stewart Macleod) from DNA extracted from normal blood cells. Systolic and diastolic blood pressure (SBP and DBP)

were gathered using a manual blood pressure cuff. Cholesterol, high-density lipoprotein cholesterol (HDL), and triglycerides (TG) were measured quantitatively using the Piccolo Lipid Panel Reagent Disc. Low-density lipoprotein cholesterol (LDL) was calculated from the determinations. Both parametric (ANOVA/t Test) and nonparametric (Kruskal-Wallis/Mann-Whitney U Test) statistical analyses were performed on blood pressure and lipid values based on their associated genotypic groupings. The tests yielding the most significant p values will be reported in the results section below. Results: The main demographics (age, height, weight, BMI) did not differ based on SLCO1B1 genotype groups (Table 1). The frequencies of SLCO1B1 genotype single nucleotide polymorphism (SNP) rs2306283 (Asp130Asn) in our postmenopausal female cohort were .3333, .4881, .1786, for GG, AG, and AA, respectively (Table 2). The corresponding frequencies of GG, AG, and AA in the 1,000 Genome Project cohort were .4044, .4281, .1675, respectively (Table 2). The frequencies of SLCO1B1 genotype SNP rs4149056 (Val174Ala) in our postmenopausal female cohort were .0119, .2262, and .7619, for CC, CT, and TT, respectively (Table 2). The corresponding frequencies of CC, CT, and TT in the 1,000 Genome Project cohort were .0169, .1692, and .8139, respectively (Table 2). The systolic and diastolic blood pressure as well as the triglyceride levels among our postmenopausal female cohort ranged from 96-192 (mmHg), 58-110 (mmHg), 42-532(mg/dL), respectively (Figure 1). We found no statistically significant associations between SLCO1B1 SNPs (rs2306283 and rs4149056) and cholesterol, HDL, or LDL. We found potentially statistically significant associations between SLCO1B1 SNP rs2306283 and SBP (p=.065) and DBP (p=.001) but not TG (p=.293), (Figures 2-4). We found potentially statistically significant associations between SLCO1B1 SNP rs4149056 and SBP (p=.041), DBP (p=.029), and TG (p=1.93E-6), (Figures 5-7). Conclusions: Our study suggests that blood pressure and triglyceride values could potentially be associated with SLCO1B1 genetics in postmenopausal females. Whether these SNPs have pathophysiological and/or treatment consequences remain to be elucidated. Further studies utilizing a sample size that fulfills all parametric requirements are necessary to confirm the possible associations drawn from our results.

Biological Sciences A – Saturday 8:00 – 9:00 Posters B – Saturday 9:15 – 10:15 Posters

(Posters designated "U" will be judged.)

1A-U. Roles for the Actin-Regulation Protein CAP1 and its Phosphorylation in Pancreatic Cancer. <u>Faith Allen</u>, Virlan Lee, Huhehasi Wu, Haitao Zhang, Dominic

Williams, Morgan Miller, Thomas J. Kelly, and Guolei Zhou. Department of Biological Sciences, Arkansas State University, Jonesboro, AR 72401.

Pancreatic cancer has the worst prognosis among major cancers, with the 5-year survival rate at a mere ~4% due to the difficulty in its early detection as well as its highly invasive nature. Development of resistance to treatments such as chemotherapy also contributes to the poor treatment outcomes. Knowledge of the molecular mechanisms behind tumorigenesis and progression of the disease is imperative before any improved treatment outcomes can be achieved. CAP1 (Cyclase-Associated Protein 1) is a key actin-regulating protein that is also implicated in the invasiveness of a variety of human cancers. Recent findings from our lab showing that CAP1 phosphorylation mediates cell signals suggest that the protein may also play roles in the proliferation of pancreatic cancer cells. We generated PANC-1 stable clones with efficient CAP1 knockdown, and found that depletion of CAP1 led to accumulated stress fibers, reduced cancer cell motility and invasion. These phenotypes were specific to CAP1 knockdown as verified through rescue experiments. CAP1 depletion also reduced the activity of ERK, a key regulator of cell proliferation. Interestingly, phosphorylation at the Ser308/Ser310 tandem site regulates both CAP1 functions in the invasiveness as well as proliferation. In summary, CAP1 likely mediates cell signals to control cancer invasiveness and unlimited cancer cell proliferation; CAP1 and its regulatory signals thus carry translational potential for the dreadful disease.

1B-USpecific betacyanins derived from dragonfruit show a lack of neuroprotective effects in neurons of the central nervous system. <u>Alyssa Hoover</u>, Todd Savolt, Lilia Koza, Aimee Winter, and Daniel Linseman. *Biology Department, Harding University, Searcy, AR* 72143.

Neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis (ALS), are characterized by the death of neurons in the brain, brain stem and spinal cord. Although little is known about the pathological mechanisms underlying these disorders, one hallmark of neurodegenerative disease is neuronal apoptosis triggered by oxidative and nitrosative stress. Betacyanins are nutraceuticals, natural products that provide medicinal benefits, such as intrinsic free radical scavenging activity and anti-inflammatory activity, which could be therapeutic in the context of neurodegeneration. In particular, we examined the neuroprotective and anti-inflammatory activity of betanin, a betacyanin derived from dragon fruit. Primary rat cerebellar granule neurons were used as the model to test neuroprotection from oxidative and

nitrosative stress. Cells were treated with sodium nitroprusside (SNP), a nitric oxide (NO) donor, alone or following 24h pretreatment with betanin and assessed for apoptosis. Results showed that apoptosis increased from untreated healthy control group to the group treated with SNP alone by almost 90%, and pretreatment with betanin had no significant effect on SNP-induced apoptosis. The anti-inflammatory effects of betanin were also examined using the BV2 microglial cell line. Microglia, the resident immune cells of the central nervous system, release NO following activation and transition to an inflammatory phenotype. The insult used to elicit an immune response was lipopolysaccharide (LPS). BV2 cells were administered LPS alone or following 24h pretreatment with betanin, and NO production was measured using the Griess method. Microglial cells treated with LPS alone showed a marked increase in NO production compared to untreated control BV2 cells, and pretreatment with betanin did not attenuate this effect. These results indicate that betanin does not have an effect on NOinduced toxicity or NO produced by activated microglia. The failure of betanin to provide neuroprotective and anti-inflammatory benefits is hypothesized to stem from its structure. Future studies will focus on comparing betanin to its derivative, betanidin, which possesses a catechol structure. Catechols are known to enhance the antioxidant activity of many nutraceuticals. Further research will be conducted using the same experimental procedure in order to determine the effectiveness of betanidin in neuroprotection.

2B-U. A First Look into the microbiome found in and on Rabidosa rabida, a spider found in Searcy, AR. <u>Patricia</u> Rivera, Ryan Stork, and Amber Hug. *Biology Department, Harding University, Searcy, AR* 72143.

Microbiome, the mass collection of microorganisms living in and on a host have been a focus of biomedical research using vertebrate and invertebrate models. In a first study, looking at spiders, we collected excreta and body swab samples from Rabidosa rabida a large wolf spider. Samples were tested using gram stain, catalase and coagulase tests while using aseptic technique. Staphylococcus aureus, Staphylococcus sp., and gram stain positive bacilli were found on the excreta samples while Staphylococcus sp., gram negative bacilli, and gram negative cocci were found on the body swabs. The majority of the excreta samples had no growth and those that did had only one type. The body swab samples grew multiple types of microorganisms that were limited to body location revealing spatial variation. Our study describes potential host-microbiome interactions using a new model with a relatively simple gut and unique characteristics such as extra oral digestion and potential antibiotic proteins. A better understanding of the factors affecting microbial-host

interactions allow us to understand more complex relationships such as those found in the human.

3A-U. Defining the Interactions Between Auxin Synthesis, Transport, and Sequestration using Chemical Inhibitors in Arabidopsis thaliana. <u>Sarah Ciesielski</u>, Rebekah Rampey, and Bethany Zolman. *Biology* Department, Harding University, Searcy, AR 72143.

Auxin is an essential hormone for regulating plant growth. This cardinal role of auxin in plants suggests that there are certain threshold concentrations of this hormone that need to be maintained in different areas of the plant to produce a desired effect on growth in those areas. The purpose of this study was to determine the interactions of auxin input pathways in maintaining auxin homeostasis. Bioassays of multiple Arabidopsis accessions were utilized using a chemical inhibitor (BUM) to study auxin synthesis, sequestration, and transport in Arabidopsis thaliana wild-type and mutant plants. The use of BUM as an auxin transport inhibitor (ATI) in this study enabled the researcher to determine how these processes are regulated differently among multiple Arabidopsis accessions by studying their growth changes. Two seedling responses were assessed and compared to the Columbia accession: primary root elongation and hypocotyl growth. Measurements were taken after eight days of incubation and compared to wild-type Columbia measurements to compute BUM sensitivities and elongation percentages on BUM versus PNS. Of the 35 accessions tested, a majority exhibited similar growth responses to that of Columbia. There were many accessions that showed signs of increased or decreased sensitivities to BUM in either the hypocotyl or primary root, and two lines have altered sensitivities in both assessed areas. It can be concluded from this study that certain natural Arabidopsis lines displayed resistance to BUM, while others showed a contrasting hypersensitivity to this compound.

3B-U. A "Tail" of an Unusual Histone H2A Variant in Bdelloid Rotifers. <u>Miracline Ebijoyeldhas</u>¹, Marjan Boerman², Alan J. Tackett³, and Andrew M. Schurko¹. ¹Department of Biology, Hendrix College, Conway, AR 72032, ²Department of Pharmaceutical Sciences and ³Department of Biochemistry and Molecular Biology, UAMS, Little Rock, AR 72205.

In eukaryotes, the nucleosome is comprised of an octamer of four canonical core histones (two copies each of H2A, H2B, H3, and H4) around which ~147bp of DNA is wrapped. Contrarily, nucleosomes in bdelloid rotifers (a class of microinvertebrates) contain unusual H2A variants with C-terminal tails ~20-40 residues longer than in other eukaryotes. While the genome project for the bdelloid Adineta vaga designated three distinct histone H2A variants, our search of the genome revealed a putative gene encoding a novel fourth H2A

variant (hereafter called "H2A-HDX"). The predicted translation of H2A-HDX is 256 amino acids; this makes it unusual in that its C-terminal tail is estimated to be over 120 residues longer than canonical H2A. The objective of this project was to characterize the sequence and function of H2A-HDX using phylogenetic, gene expression and mass spectrometry analyses. First, a phylogenetic analysis including H2A variants from other animals was done. This demonstrated that H2A-HDX represents a unique lineage of H2A variants distinct from other H2A sequences of other animals and those of bdelloid rotifers. We then used reverse transcription PCR and rapid amplification of cDNA ends (RACE) to validate that the H2A-HDX gene transcript includes the C-terminal tail. Since certain H2A variants (such as H2AX) function in DNA repair in other eukaryotes, we wanted to determine if H2A-HDX performed a similar role. We used real-time PCR to quantify expression levels of H2A-HDX in irradiated and non-irradiated samples. However, we found the expression of H2A-HDX (and other H2A Variants) in irradiated samples was not elevated relative to non-irradiated samples, suggesting that upregulation is not associated with DNA repair. Finally, to validate the predicted translation of H2A-HDX, we isolated histones from A. vaga. Highresolution mass spectrometry identified H2A-HDX, and validated the first 194 of the predicted 256 amino acids, and several post-translational modifications (PTMs) were also identified. This variant also comprised a very small component of the overall histone population, which could explain the low validation number of the H2A-HDX gene. Future studies examining PTMs of this protein and the effects of deleting the H2A-HDX gene (using CRISPR-Cas9 genome editing) could shed light on the role of this unusual histone variant in DNA repair or other cellular processes in bdelloids.

4A-U. MAPK Inhibition Reduces Motility of Papillary Thyroid Cancer Cells Harboring BRAFV600E Mutations.

<u>Will Gibson</u>, Roshaneh Ali, LeeAnn Jolly, Aime T. Franco, Laura J. MacDonald. *Biology Department, Hendrix College, Conway, AR* 72032.

Thyroid cancer is the most common endocrine cancer in the United States and incidence is expected to exceed that of colon cancer by 2030. The two most common types are follicular and papillary thyroid cancer. Follicular thyroid cancer, which metastasizes to the lungs and bones, is commonly associated with mutations in the HRAS gene. Papillary thyroid cancer, which metastasizes to the lymph nodes, is commonly associated with mutations in the BRAF gene. Interestingly, BRAF lies directly downstream of HRAS in an important signaling cascade that contributes to cancer initiation, proliferation, and motility, yet mutations in these linked oncoproteins lead to distinct differences in pathology and metastasis. In this study, we tracked movement and morphology of cells derived from mouse thyroid tumors harboring either the BRAF

or HRAS mutations in combination with PTEN deletions using time-lapse microscopy to determine whether these genetic mutations result in altered motility important for metastasis. While we observed little difference in overall motility, our data suggests that cells collected from tumors with BRAF mutations display significantly reduced rates of motility when treated with an inhibitor targeting MAPK signaling pathways downstream of BRAF. Additionally, these cells become more epithelial in appearance, suggesting activation of the MAPK signaling pathway is critical for papillary thyroid cancer progression.

4B-U. Bdelloid rotifers and meiotic proteins: The untold story of an ancient asexual lineage. <u>Jeanita C.</u> <u>McReynolds</u>, Alan J. Tackett, and Andrew M. Schurko. *Biology Department, Hendrix College, Conway, AR* 72032.

Bdelloid rotifers are a class of aquatic microinvertebrates that have seemingly flourished for over 40 million years without sex, meiosis, or males. The long-term success of this ancient ameiotic lineage is attributed, in part, to the extraordinary ability of bdelloids to repair DNA double strand breaks induced by desiccation. Despite the longstanding absence of meiosis in bdelloids, their genomes contain four genes that code for proteins (SPO11, HOP1, MSH4, MSH5) specific to meiosis in other eukaryotes. Since bdelloids lack meiosis, the objective of this project is to investigate the function of meiotic proteins in bdelloid rotifers and the potential role of these proteins during DNA repair. We first performed western blot assays using custom antibodies for SPO11, HOP1, MSH4 and MSH5 to confirm that their corresponding genes were expressing proteins in the bdelloid Adineta vaga. To characterize binding partners of these meiotic proteins, protein pull-down assays were then done. We generated 6×histidine-tagged copies of each meiotic protein (and also of DNA repair proteins RAD51 and MRE11) and these were used in pull down assays using Dynabeads and protein lysates from A. vaga. SDS-PAGE is being used to identify potential binding partners, which will be further characterized by mass spectrometry. Our next goal is to determine the binding partners of these meiotic proteins in irradiated bdelloids to determine if these proteins are involved in DNA repair. Overall, this study aims to determine if meiotic genes in bdelloids have evolved a novel non-meiotic function, which would justify the maintenance of these genes in an ameiotic lineage and further our understanding of DNA repair in eukaryotes.

5A-U. Growth Conditions Impact Tunneling Nanotube Production in Mouse Thyroid Cancer Cell Lines. Braxton Anderson and Aime T. Franco, Biology and Biophysics Departments, Hendrix College, Conway, AR 72032 and UAMS, Little Rock, AR 72205.

Tunneling nanotubes (TNTs) are microscopic structures that have recently emerged as a new mode of communication between cells. These TNTs are actinbased, versatile structures that are long, non-adherent and connect distant cells to permit the direct intercellular transfer of diverse components. TNTs role in cancer was first hypothesized when a study confirmed the presence of oncogenic miRNAs being transported by the TNT. Additionally, research has found that a higher than average TNTs/cell is associated with invasive malignant mesothelioma compared to less aggressive subtypes. The purpose of this project was to assess the average number of TNTs/cell in cancer lines with distinct oncogenic mutations that drive tumorigenesis. The research was conducted with cancer cells that had one of three independent Braf cell lines or from cancer cells that had one of three independent Hras cell lines. Furthermore, we used 3 different growth conditions to determine what effect different microenvironments may have on TNT formation. Cells were first compared between growth on tissue culture plates or plates coated with collagen. We next sought to determine whether inhibition of Mek would inhibit TNT formation on cells grown on tissue culture plastic. We hypothesize that cells with the Hras mutation will have a higher average TNT/cell than that of Braf mutations and that growth on collagen will induce TNT formation. In order to test this hypothesis, cell motility videos were taken of the various samples in different growth conditions. We then quantitated the number of TNTs/cell that were visualized at 15 minute intervals during the course of the 4 hour video. We found that more TNTs in Hras cells compared to Braf cells and that collagen increases TNT production.

5B-U. Assessing the Efficacy of MAPK, AKT, and mTOR Inhibitor Treatments in Novel Cellular Models of Papillary and Follicular Thyroid Cancer. <u>Brianna</u> <u>LeBoeuf</u>, <u>Maggie Young</u>, Anna Sharabura, Benjamin Zamzow, LeeAnn Jolly, Aime T. Franco, and Laura J. MacDonald. *Department of Biology, Hendrix College, Conway, AR* 72032.

Thyroid cancer is the most common endocrine malignancy, and incidence of thyroid cancer has been steadily increasing since the 1970s. Worldwide incidence is expected to exceed that of colon cancer by 2030. The most common types of thyroid cancer are papillary thyroid cancer and follicular thyroid cancer, each of which is associated with different genetic mutations, pathology, and metastasis. Activating BRAF mutations are most commonly found in papillary thyroid tumors while activating HRAS mutations are most commonly found in follicular thyroid tumors. Thyroid cancer is typically treated through surgical removal of the thyroid and radioactive iodine ablation of remaining tumor cells. Conventional treatment is nearly 99% effective for individuals with well differentiated cancer, however, patients receive lifelong thyroid hormone replacement therapy, which is often suboptimal and results in reduced quality of life. Additionally, this approach is not effective for individuals with poorly differentiated or anaplastic thyroid cancer, and there are few chemotherapeutics available for these patients. Collectively, these observations highlight a need for increased evaluation of inhibitors for development of chemotherapies. In this study, we sought to evaluate the effects of MAPK, AKT, and mTOR inhibitors on cellular proliferation in cellular models of papillary and follicular thyroid cancer. We determined accurate IC50 concentrations for these inhibitors using the recently reported GR50 metric, a technique which calculates IC50 concentrations correcting for cellular growth rates. Additionally, we noted that these inhibitors were more effective used in combination than as monotherapies. We also assessed the efficacy of alternating their use to potentially reduce cytotoxicity that would be anticipated with combination drug therapy.

6A-U. Transcriptome Analysis Reveals a Message During DNA Repair in Bdelloid Rotifers. <u>Christa C.</u> <u>Huber</u>, Galina V. Glazko, Yasir Rahmatallah, Marjan Boerma, and Andrew M. Schurko. *Department of Biology, Hendrix College, Conway, AR* 72032.

Bdelloid rotifers are microscopic aquatic animals that have apparently survived for more than 40 million years without sex, males, or meiosis. Bdelloids have an efficient DNA repair system that gives them the ability to recover from levels of ionizing radiation that are lethal to other eukaryotes. DNA double strand breaks induced by high doses (>1000 Gray) of ionizing radiation are repaired without significant loss of viability to the organism. The objective of this project is to characterize genes that are differentially expressed in the bdelloid Adineta vaga following exposure to ionizing radiation in order to gain insight into mechanisms of DNA repair. Transcriptome sequencing was carried out on RNA isolated from irradiated cultures of bdelloids (280 Gray total dose followed by a 30 minute recovery) and from non-irradiated controls. From this data, 567 genes were differentially expressed with 268 of the genes being upregulated and 298 downregulated in the irradiated bdelloids. Real-time PCR (RT-PCR) was done to validate the upregulation of a DNA ligase homolog, and other differentially expressed genes are being targeted with RT-PCR to validate the transcriptome data. Gene ontology enrichment analysis was carried out to identify biological processes that were differentially regulated in irradiated bdelloids. Interestingly, 131 of the 567 (23.1%) differentially expressed genes appeared to lack homologs in other eukaryotes. However, a BLASTX search of regions flanking these genes revealed that 93 of the 131 likely have homologs but their annotations are incomplete. The remaining 38 differentially

expressed genes appear to be specific to bdelloids. For poorly annotated genes, random amplification of cDNA ends (RACE) is being done. For example, we characterized the sequence of a previously unannotated map kinase homolog that was only expressed during DNA repair. Future work will involve carrying out transcriptome sequencing of bdelloids at two additional time points (0 and 60 minutes) post-irradiation to highlight changes in gene expression during a broader timeframe following DNA damage. Overall, this ongoing gene expression analysis has identified several candidate genes for having functions in DNA repair, which will provide further insight into the mechanism of DNA repair in bdelloid rotifers.

6B-U. Improving Inflammation in Viral Bacterial **Coinfection by II-1β Regulation.** <u>Angeline Rodriguez</u>, Abbi Mabary, Andrea Taylor, Hannah Ingram, and Christopher Lupfer. *Department of Biology, Missouri State University, Springfield, MO* 65897.

Viral bacterial coinfections are known to cause severe pneumonia, especially in the elderly and in pediatric patients. Antibiotics like β -Lactams kill the bacteria but fail to improve symptoms suggesting a faulty immune system may play an important role in the disease. Interlukine-1 β (IL-1 β) is an important immune signaling cytokine responsible for inflammation. It exists as an inactive precursor that can be activated by Caspase-1 containing inflammasomes (multi-protein complex). Influenza A virus and Streptococcus pneumoniae activate the inflammasome through the NOD-like receptor protein NLRP3. Previous reports indicate that IL-1β levels are dramatically elevated during coinfection with Influenza A virus and Streptococcus pneumoniae. However, how IL-1β levels increase and their importance in coinfection is not known. We have discovered that IL-1 β expression and secretion is increased during coinfection as a result of activation of multiple signaling pathways simultaneously. This was concluded in experiments where macrophages deficient in the Myd88-/-, AIM2-/- or Nlrp3-/- genes were examined for their effects on IL-1 β augmentation. We are currently working on gaining better understandings of increased IL-1β production through in vivo experimentation using knockout Myd88-/-, AIM2-/- and Nlrp3-/- mice. In addition, we are also experimenting on treatment options using the same knockout mice and a combination of drugs including IL-1 β inhibitors.

7A-U. Generation of Yeast-2-Hybrid Clones to Examine the Role of Nucleotide Oligomerization and Binding Domain (NOD)-Like Receptors. <u>Abbi J. Mabary</u>, Hazar M. Abysalaman, Angeline E. Rodriguez, and Christopher Lupfer. *Department of Biology, Missouri State University, Springfield, MO* 65897.

NOD-like receptors (NLRs) are a class of cytoplasmic proteins essential for the initiation and regulation of immune responses to infectious disease, metabolic and cellular damage and cancer. The human genome encodes for 22 NLR proteins. However, only about half of the 22 NLRs have known functions, and the mechanisms by which they function are even more ambiguous. Previous research indicates that some NLRs activate inflammation, while others, like NLRP12, functions as regulators of inflammation, thus serving as a negative feedback mechanism. NLRP12 suppresses inflammation by inhibiting the transcription factor NF"kB", which activates transcription for cytokines that activate the immune response cascade. Inhibition of NFkB by NLRP12 is important in the prevention of a hyper-inflammation, which is involved in severe infections as well as cancer development. Although the general function of NLRP12 is known, how it is activated is not known. We are, therefore, embarking on a journey to find novel proteins that interact with NLRP12 in an effort to decipher the mechanisms by which they function. We are generating a yeast 2-hybrid system to examine the interaction of NLRP12 with a human cDNA library. Novel interactions discovered through this 2hybrid screen should provide insight into the function of this NLR protein and help us understand the immune response to infectious and non-infectious diseases.

7B-U. Subcellular Targeting and Physiological Significance of Dynamin-like Protein, Vps1. John Short and Kyongtae Kim. Biology Department, Missouri State University, Springfield, MO 65897.

Dynamins are required for proper protein sorting, and their dysfunctions are linked to Alzheimer's disease. Defects in yeast dynamin Vps1 are associated with dysregulation of multiple pathways of membrane trafficking. Interaction of Vps1 with membrane lipids of Golgi bodies and endosomes was previously shown, but the validity was not tested and the biochemical mechanisms of Vps1 targeting to them remain poorly understood. To investigate the mechanism, full-length Vps1 and its truncated versions, including GTPase, Mid, GED, a presumable PRD, GTPase+Mid, and Mid+GED domains, were tagged with mRFP and expressed in vps1^Δ background. Then, markers of endocytic sites, late Golgi, and late endosomes were tagged with GFP. The extent of colocalization of GFP markers with mRFPfused Vps1 and its fragments was examined using fluorescence microscopy. Surprisingly, we found that the mRFP-fused Vps1, previously known as an endocytic factor, did not show colocalization with endocytic sites, refuting previous publications. However, Vps1 overlaps with endosomal and Golgi puncta as expected, albeit only full-length. Furthermore, the truncated Vps1 fragments were not functional for CPY sorting at the Golgi or the retrieval process of the CPY receptor Vps10

toward the Golgi. These suggest that full-length Vps1 protein is essential for its proper targeting and function.

8A-U. Alterations in Hemodynamic Loading leads to Morphological Changes of the Heart in Developing Mouse Embryos. <u>Tanner Hoog</u>, Samantha Fredrickson, and Ryan Udan. *Biology Department, Missouri State University, Springfield, MO* 65897.

Congenital heart defects are aberrations to normal heart development that can have very serious implications in the health of children. Emerging studies indicate that the mechanical force created by the flow of blood (also called hemodynamic loading) can play a role in proper heart development. For example, previous experiments on zebrafish and chick embryo models indicate that altered blood flow impairs heart morphogenesis on a physiological and cellular level (Sedmerra et al., 1999; Hove et al., 2003), but little is known about how flow affects mammalian heart development. Utilizing hemodynamic manipulation techniques previously found to work in mouse embryos (lucitti et al., 2007), we seek to assess how alterations in mechanical force affects mammalian heart development. Using OPT microscopy we are assessing structural changes of the heart, specifically looking at volume, myocardial thickness, and the extent of trabeculation. Further research needs to be conducted on a cellular scale to better explain these changes. Thus, the next step is to perform immunostaining techniques to look for changes in heart cell (cardiomyocyte or endocardial cells) proliferation, alignment, and presence/absence of monocilia. We hope that elucidating the structural and cellular responses to altered force will provide new insight into how congenital heart defects arise in mammals and provide guidance for establishing ways to correct this disease is humans.

8B-U. Metabolically Engineered Gluconobacter oxydans for The Production of Optically Pure Acetoin: A Pharmaceutical Precursor. <u>Neil Bolduc</u> and Paul Schweiger. *Biology Department, Missouri State* University, Springfield, MO 65897.

Gluconobacter oxydans belongs to a distinct group of acetic acid bacteria known for their unique ability to incompletely oxidize substrates under normal growth conditions, releasing products into the medium. This feature is biotechnologically relevant as the incompletely oxidized products are often stereo- and regio-selective. This unique metabolism is dependent on membrane-bound dehydrogenases that channel electrons from substrates into the respiratory chain. These dehydrogenases are natural biocatalysts that simplify the production and recovery of enantiopure chemicals, which normally require expensive and troublesome organic chemistry to produce, providing a route to sustainable green chemical biomanufacturing. One aim is to metabolically engineer G. oxydans for the production of enantiopure acetoin. Acetoin was designated a top 30 platform chemical by the US DOE and is used to produce pharmaceuticals, cosmetics, food flavorings, and liquid composites. Two G. oxydans enzymes are predicted to be important for acetoin production: 1) a known PQQ-dependent polyol dehydrogenase (SldBA), and 2) an uncharacterized FADdependent sorbitol dehydrogenase (mSDH). To rationally design G. oxydans for enantiopure acetoin production we are investigating the role of mSDH in biomanufacturing by analyzing deletion mutants and expression strains. This information will be used to produce strains for improved sustainable green chemical biomanufacturing of enantiopure acetoin.

9A. Yeast Membrane Lipid Imbalance Leads to Trafficking Defects toward the Golgi. <u>Sara E.</u> <u>Woodman</u>, Justin Conover, Chris Trousdale, and Kyoungtae Kim. *Biology Department, Missouri State University, Springfield, MO* 65897.

Protein recycling is an essential cellular process that involves endocytosis, intracellular trafficking, and exocytosis. It has been shown in mammalian systems that membrane lipids, including cholesterol, sphingolipids, and phospholipids, play a pivotal role in protein recycling. In order to address this role in budding yeast, Saccharomyces cerevisiae, we utilized GFP-Snc1, a v-SNARE protein serving as a fluorescent marker for faithfully reporting the recycling pathway. Here we show results that display moderate to significant GFP-Snc1 recycling defects upon overexpression or inactivation of phospholipid, ergosterol, and sphingolipid biosynthesis enzymes, indicating that the homeostasis of membrane lipid levels is prerequisite for proper protein recycling. Through using a truncated version of GFP-Snc1 that cannot be recycled from the plasma membrane, we determined that abnormalities in Snc1 localization in membrane lipid overexpression or underexpression mutants are not due to defects in the synthetic/secretory pathway, but rather in the recycling pathway. We found that membrane lipid imbalance resulted in an accumulation of the late endosome marker Vps10-GFP, indicating trafficking from the endosomes to the Golgi may be being blocked, preventing recycling to the plasma membrane. To elucidate the possible mechanism for this trafficking blockage, we stained the actin cytoskeleton, then quantified the percentage of cells with visible actin cables. Compared to wild-type cells, membrane lipid mutant cells exhibited lower levels of actin cables, indicating the actin cytoskeleton is disrupted upon membrane lipid imbalance. Taken together, these results show that impairment of proper recycling may be due to disruption of the actin cytoskeleton, which

causes trafficking blockage between the endosomes and Golgi. The potential mechanisms of actin cytoskeleton disruption are currently being studied.

9B. Yeast dynamin for the fusion of endosome-derived vesicles at the Golgi. <u>Pelin Makaraci</u> and Kyoungtae Kim. *Biology Department, Missouri State University, Springfield, MO* 65897.

Membrane recycling is an important cellular process required for cell homeostasis. Lines of evidence demonstrated that Vps1, a dynamin homologue in yeast, is implicated in protein recycling from the early endosome to the late Golgi. The present study reveals that Vps1 physically interacts with Ypt6, a master GTPase in the recycling pathway. It was found that two presumable inactive ypt6 mutants (Ypt6 G139E and Ypt6 T24N) and a constitutively active mutant (Ypt6 Q69L) interact with Vps1, indicating that the interaction of Vps1 with Ypt6 does not depend on the status of Ypt6 activity. Cells lacking Ypt6 displayed a severe defect in Snc1 recycling, and the abnormal phenotype was rescued by overexpression of Vps1, but not vice versa. It is, therefore, most likely that Vps1 functions downstream of Ypt6. Additionally, overexpression of Vps1 GTPase mutants was not sufficient enough to rescue the abnormal phenotype in ypt6∆, suggesting a pivotal role of GTP binding and hydrolysis for Vps1 function in Snc1 retrieval toward the Golgi. Moreover, we found that Vps1 interacts with two SNAREs, Vti1 and Snc2, essential for endosome-derived vesicle fusion with the late Golgi, pointing to a novel role of Vps1 in the late stage of the endosome-to-Golgi traffic.

10A. Vps1 functions with the GARP tethering complex for endosome -to- Golgi traffic. <u>Uma Saimani</u>, Jared Smothers, and Kyoungtae Kim. *Biology Department, Missouri State University, Springfield, MO 65897.*

Vacuolar Protein Sorting 1 (Vps1), a yeast homolog to human Dynamin, has been implicated in recycling cellular traffic from the endosome to the Golgi network. Previous research showed a genetic interaction of Vps1 with Vps51, a component of the GARP tethering complex, which anchors vesicles at the late Golgi membrane. We used the yeast two-hybrid system and pinpointed that a 33 aa segment of Vps51 interacts with Vps1. On aligning the sequences of Vps51 and Ang2, the mammalian homolog of Vps51, a conserved region was identified in the 33 aa segment, within which we created two individual point mutations which led to elimination of the interaction between Vps1 and Vps51. Colocalization was observed between Vps1 and Vps51 in a wild type cell, and the absence of Vps1 resulted in reduced colocalization of Vps51 with a Golgi marker. Vps51 is known to interact with Tlg1, a SNARE protein, and we observed that lack of Vps1 also led to mislocalization of Tlg1. Further, our functional analysis

revealed that Vps1 acts upstream of Vps51 for endosome-to-Golgi traffic. Together, we propose that Vps1 functions together with the GARP tethering complex to facilitate the vesicular traffic toward the Golgi.

10B. Yeast dynamin Vps1 associates with clathrin to facilitate vesicular trafficking and controls Golgi homeostasis and shuffling. <u>Mariel Delgado Cruz</u>, Shiva Kumar Goud Gadila, Uma Saimani, Michelle Williams, Pelin Makaraci, and Kyoungtae Kim. *Biology Department, Missouri State University, Springfield, MO* 65897.

The yeast dynamin Vps1 acts cooperatively with many proteins at diverse cellular locations for endocytosis, protein sorting, and membrane fusion and fission. It has been proposed that Vps1 is functionally linked to clathrin heavy chain 1 (Chc1), but the question of how, where, and when they function together remains unknown. Here, we report that Vps1 arrives at the Golgi after clathrin, and that loss of Vps1 leads to a shift in the cellular localization of clathrin to the late endosome and vacuole, not vice versa. Our two-hybrid-based approach provides evidence that full-length Vps1 and its truncated versions bind to the C-terminal region of the Chc1. Cells lacking both Vps1 and Chc1 displayed more severe defects in carboxypeptidase Y (CPY) sorting at the Golgi than those in Vps1-deficient cells. Further, these Vps1 fragments became dominant-negative for CPY sorting upon overexpression. These results suggest that Vps1 binds to Chc1 and functions together at the Golgi for efficient Golgi-to-endosome membrane trafficking. In addition, we found that Vps1, without the aid of clathrin, plays a role in controlling the number and turnover of late Golgi.

11A. The Effects of Single Walled Carbon Nanotubes on Diamondback Moth Feeding, Growth, Pupation, Survival and Fecundity. <u>Taiaba Afrin</u> and D. Alexander Wait. *Biology Department, Missouri State University,* Springfield, MO 65897.

Engineered nanomaterials are widely used in industry, technology and medicine and their usefulness now and in future is absolute. However, the potential adverse effects on organisms has not been well studied. Carbon Nanomaterials (CNTs) are one of the most widely used nanomaterials in consumer products because of their unique properties. The goal of our research is to identify direct and indirect effects of single walled carbon nanotubes (SWCNTs) on Diamondback Moth (DBM, Plutella xylostella) feeding, growth, pupation, survival and reproduction. To date, we have assayed SWCNTs in trials with second and third instar DBM larvae. To assay for direct effects, we ran artificial food assays with the following concentrations: 8.64 mg/L, 17.28 mg/L, 34.56 mg/L, 69.12 mg/L and 138.24 mg/L CNTs. Across six

trials, consumption was statistically marginally significantly affected (ANOVA: p = 0.056), while growth was significantly affected (ANOVA: p = 0.030). Results from assays suggest that CNTs are reducing the pupation (ANOVA: p = 0.010) and fecundity (ANOVA: p =0.041) rates as CNT concentration increases, but there is no effect of CNT\on survival rates (ANOVA: p = 0.108). Our research to date suggests that pure CNTs have some unique mechanistic effect in the gut of the insect that affects fecundity. Future research will determine the mechanisms for CNT effects (positive, neutral, or negative).

11B. Investigating the effects of high and low hemodynamic loading on mouse embryonic heart development. <u>Samantha Fredrickson</u>, Tanner Hoog, and Ryan Udan. *Biology Department, Missouri State University, Springfield, MO* 65897.

The most common type of birth defects are congenital heart defects (or CHDs) (National Institutes of Health). Though a few cases of CHDs have been attributed to genetic defects specific to the heart, or to maternal disease (eg. diabetes), the cause of most CHDs is unknown (American Heart Association). Thus, further research is needed to determine how CHDs form. Very few studies have investigated how physiological factors like perturbations of blood flow can affect normal heart development. For instance, increasing or decreasing the hemodynamic load can change the morphology and function of the heart in both zebrafish and chicken embryos (Culver and Dickinson, 2010). This could be one way to explain how CHDs form, but further investigation in a mammalian system is needed. To examine this idea, we are experimentally manipulating cultured mouse embryos and testing the effects of increasing or decreasing blood viscosity (to increase or decrease hemodynamic loading). To determine any effects on heart development, we are preparing embryos for 3D imaging by optical projection tomography (OPT), and have begun morphometric analysis to compare heart morphologies. Further, we will determine if high or low resistance to flow will also alter the expression of heart genes by RNA sequence analysis. As of now, we have successfully prepared normal hemodynamic load and low hemodynamic load embryos for imaging by OPT, and are manipulating the embryos for increased hemodynamic load.

12A. The effect of hemodynamic force on the maturation of blood vessels during embryogenesis. <u>Rachel Padget</u>, Shilpa Mohite, Tanner Hoog, and Ryan Udan. *Biology Department, Missouri State University, Springfield, MO* 65897.

Throughout embryonic development, blood vessels are derived from endothelial cells by way of vasculogenesis. These vessels then remodel to form a hierarchy of largediameter arteries that branch into small-diameter capillaries during angiogenesis. As vessels continue to remodel, they undergo maturation, whereby the vessels respond to signaling events to become surrounded with an outer layer of vascular smooth muscle cells (vSMCs). This results in large-diameter, proximal arteries that have a thicker vSMC layer than small-diameter, distal capillaries. However, it is unclear why arteries have a thicker vSMC layer than capillaries. Previous studies have implicated that mechanical forces provided by blood flow control the formation of arteries over capillaries, we hypothesize that these mechanical forces may also determine the extent of vSMC coverage. To test the hypothesis, we compared the extent of vSMC coverage in arteries from normal-flow embryos (wild type) with arteries from reduced-flow embryos (MyI7-/mutant embryos having reduced heart contractility, and thus reduced hemodynamic force). We observed less vSMC coverage in the arteries from reduced-flow embryos. To ascertain the cause of reduced vSMC coverage, we speculated that hemodynamic force may promote either the recruitment, differentiation or proliferation of vSMCs. By performing immunostaining and confocal imaging, we determined that vSMCs were present in reduced-flow embryos, but they failed to migrate away from capillaries towards arteries, and failed to surround the arteries. This implicates that hemodynamic force is required for vSMC recruitment, but not for vSMC differentiation or proliferation. Further, flow cytometry revealed an increase in the number of vSMCs in reduced-flow embryos. This observation correlates to a phenomenon whereby adult vSMCs can undergo phenotypic modulation. We hypothesize that during embryogenesis, hemodynamic force controls this balance such that areas of high hemodynamic force promote the attachment of vSMCs; whereas, areas of low hemodynamic force allow for the continued proliferation of vSMCs.

12B. Sodium Pyruvate Alters the Immune Response to Influenza A Virus Infections in Macrophages. <u>Hazzar</u> <u>Abysalaman</u> and Christopher Lupfer. *Biology Department, Missouri State University, Springfield, MO* 65897.

Sodium Pyruvate Alters the Immune Response to Influenza A Virus Infections in Macrophages Hazar Abysalamah. Faculty Mentor: Dr. Christopher Lupfer Department of Biology, Missouri State University, Springfield, MO 65897 Pyruvate is the end product of glycolysis. It can either be transported into the mitochondria for use in the TCA cycle or be used to regenerate NAD+ during aerobic glycolysis. We recently discovered that addition of sodium pyruvate to the culture medium during infection of macrophages with influenza A virus affects the production of cytokines involved in immune signaling. We hypothesized that sodium pyruvate may directly inhibit the virus. Alternatively, sodium pyruvate involved in energy production in the macrophages may alter the immune response to the infection. While infection of macrophages with influenza A virus resulted in high levels of cytokines (IL-6, IL-1 β , and TNF- α) in the absence of sodium pyruvate, the addition of sodium pyruvate significantly impaired cytokine production. Furthermore, sodium pyruvate did not affect virus growth, suggesting the effect of sodium pyruvate is on the immune response produced by the macrophages and not the viability of the virus.

13A-U. Bacteriocin Produced by Halobacteria from White Sands, NM Inhibits MRSA. <u>Yuliya Kunz</u> and Ratnaker Deole. *Natural Sciences Department, Northeastern State University, Tahlequah, OK 74464.*

Antibiotic resistant bacteria fleetly disseminate around the globe posing a major issue to the humanity by threatening the efficiency of currently available antibiotics. Such super-bug as Methicillin-resistant Staphylococcus aureus (MRSA) is especially concerning due to its fast mutation rates which significantly reduces the amount of potent antibiotics against it. As a result, current antibiotics rapidly become ineffective before new ones are found, which leaves the community vulnerable. MRSA alone is responsible for over 11,000 deaths in the U.S. each year. Resistance of MRSA and other super-bugs is attributed not only to the misuse of antibiotics but also the development of antibiotic resistance in nature, resulting from MRSA's frequent exposure to particular antimicrobial compounds within the same environment. Therefore, logical places to look for new potent antibiotics against MRSA would be environments that MRSA is not likely to inhabit. One of such environments is hypersaline ecosystem - the home for wide variety of halophilic microorganisms belonging to all three domains of life. Some halophiles have been previously found to produce antimicrobial compounds. We hypothesize that hypersaline environments such as White Sands in New Mexico harbor halophilic bacteria that produce antimicrobial compounds (bacteriocins), possibly for nutrient competition elimination purposes, which are active against MRSA. Antibiotic susceptibility assay was used to determine the domain of isolated microorganisms, as well as antibiotic sensitivity assay to establish whether isolated microorganism produces antimicrobial compounds. Protease test helped determine the nature of antimicrobial compound isolated, whereas, exclusion chromatography, molecular weight cut off filtration, Tricine gel electrophoresis, and contact bioassay were used to determine the size of the isolated antibiotic. White Sands sample showed the presence of bacteria producing bacteriocin of proteinaceous nature approximately 53 kDa in size. This bacteriocin have been found capable of inhibiting the growth of MRSA in the medium of 0.5M NaCl minimal concentration. According to our results isolated

bacteriocin is active against MRSA and its further characterization would help to acquire better understanding of its mechanisms of action against MRSA, which could potentially lead to development of novel antibiotic effective against this notorious superbug.

13B. Exploring the Mcm10 and Mrc1 Interaction at the Replication Fork. C. Hendrix, B. Fultz, <u>Casey Eddington</u>, and S. Das-Bradoo. *Natural Sciences Department, Northeastern State University, Tahlequah, OK* 74464.

Accurate replication of the genome requires the evolutionarily conserved minichromosome maintenance protein, Mcm10. Mcm10 is a multifunctional replication factor with reported roles in origin activation, polymerase loading, and replication fork progression. It carries out these functions through its interaction with numerous proteins such as Mcm2-7 core helicase, the lagging strand polymerase, DNA polymerase- α and the replication clamp, proliferating cell nuclear antigen. Loss of these interactions caused by the depletion of Mcm10 leads to chromosome breakage and cell cycle checkpoint activation. The literature supporting these roles is controversial, and it has been debated whether Mcm10 has an active role in elongation. To gain insight into this function of Mcm10, we studied its interaction with the mediator of replication checkpoint 1 (Mrc1) and Toposiomerase 1 interacting factor (Tof1). These proteins have been identified as replication checkpointspecific mediators in budding yeast, and also as components of the replisome progression complex. Interestingly, we observed that Mcm10 does not interact with Tof1, but shows a robust interaction with Mrc1 by yeast-two hybrid assays. Furthermore, this interaction is independent of the checkpoint function of Mrc1. Co-immunoprecipitation experiments suggest that this interaction occurs throughout the cell cycle and is independent of DNA. Furthermore, mutational analysis has revealed that Mcm10 interacts through the conserved C-terminus region of Mrc1. Currently, we are conducting experiments to further elucidate this interaction. Our results suggest that Mcm10 interacts with Mrc1 to facilitate replication fork progression.

14A-U. Inclusion body and periplasmic transgenic expression of blood clot dissolving proteins. <u>Sawyer</u> <u>Sparks</u> and Kevin Yeuju Wang. Natural Sciences Department, Northeasern State University, Tahlequah, OK 74464.

The formation of a blood clot in the circulatory system can cause potentially a fatal heart attack or stroke. Lumbrokinases, found in earthworms, and Nattokinase, found in Bacillus subtilis for soybean fermentation, both expresses medicinal fibrinolytic activities without excessive bleeding to combat thrombotic associated diseases. Our goal is to clone codon optimized Lumbrokinase (PI239) and Nattokinase (Genbank: AF368283.1) as an inclusion body, and as periplasmic proteins with a leader sequence (peIB). Polymerase chain reaction (PCR) was used to amplify genes PI239 and NATTO that were synthesized by Genscript Co. The DNAs were isolated and inserted into a single-vector DNA replicon system, PEt-22b (Novagene Inc.), vector for expression of the recombinant protein in Escherichia coli. The genes were chemically transformed into the E. coli cells (NEB 5-alpha), constructed plasmid harvested and transformed into new E. coli cells (NEB BL21). Gene of interest was expressed using magic media (Invitrogen) and protein purified. The future prospects would be to confirm the expression and retention of the anti-thrombolytic activity associated with the genes of interest through protein analysization and fibrin dissolving assay.

14B. Mcm10 interacts with Polymerase Epsilon and May Coordinate DNA Replication and the S-phase Checkpoint Pathway. <u>Brandy Fultz</u>, Casey Eddington, and Sapna Das-Bradoo. *Natural Sciences Department, Northeastern State University, Tahlequah, OK* 74464.

A hallmark of cancer is a high rate of mutations and genome instability caused by genetic changes. Many of these changes are caused by errors during DNA replication. To prevent such errors, cells have evolved replication stress (S phase) checkpoint, a mechanism that slows replication in response to lesions that are difficult to replicate. Although the stress response pathway is understood fairly well, there is an outstanding issue as to how it is activated. It has been suggested that replication proteins may be involved in this checkpoint activation process. Two independent genome-wide screens for factors that maintain chromosome integrity identified minichromosome maintenance protein 10 (Mcm10) as one of the few replication proteins that are highly effective in preventing DNA damage. However, how Mcm10 promotes normal S phase progression and prevents DNA damage is still an open ended question. Here, we show that Mcm10 functions in replication and S phase checkpoint pathways in Saccharomyces cerevisiae through its interaction with Polymerase epsilon (Pole). Yeast two hybrid results from our laboratory show a robust interaction between Mcm10 and Pol2, the catalytic subunit of Pole. Interestingly, Mcm10 interacts with the C-terminus domain of Pol2, a domain that participates in S phase checkpoint activation. In addition, we have mapped the interaction of Mcm10 to a 200 amino acid region within the checkpoint domain of Pol2; we are presently carrying out site-directed mutagenesis to further narrow this site of interaction. To substantiate the yeast two hybrid, we have confirmed the physical interaction of Mcm10 and Pol2 through co-immunoprecipitation. Interestingly, we have verified that the interaction is cell cycle regulated; it first appears in early S phase and persist through S and G2 phases. Currently, we are conducting experiments to investigate if this interaction changes under replication stress and DNA damage conditions. Our data sheds new light on the function of Mcm10 in DNA replication and S phase checkpoint pathways.

15A-U. Testing Efficacy of Disposable Lab Coats. Levi Mounce, Jose Hernandez, Anthony Kyle Maddox, Cameron Pervis, Jordan Slater, and LaShall Bates. *Biology Department, Northwest Arkansas Community College, Bentonville, AR 72712.*

Microbes have the capability of surviving on textiles, yet they are used to protect individuals in laboratory settings. One major concern is the contamination of student clothing while participating in a microbiology class. This study investigated the efficacy of using disposable lab coats in a microbiology classroom. Disposable lab coats offer low cost and ease of disposal when contaminated. Disposable lab coats composed of differing materials were inoculated with Serratia marcescans and incubated to simulate a time lapse. The samples were then tested using modified dilution plates to determine the amount of growth on the fabrics within 24 hours. A study was also conducted to determine if normal handling of these types of material would result in inoculation. Ignition and incineration tests were also conducted.

15B-U. Effects of Pythium species on Biofumigant Potential Mustard Plants. <u>Amber Lancaster</u>, Levi Mounce, Jack Outlaw, and Gary Bates. *Biology Department, Northwest Arkansas Community College, Bentonville, AR 72712.*

Pythium species are the cause of Pythium damping-off and root rot. This soil born disease is a common early season problem in cool soils in the state of Arkansas affecting various agronomic and horticultural crops. This infection kills seedlings and forces producers to replant. One method to control Pythium spp. and the resulting diseases is biofumigation. Biofumigation is the process of using Brassica residues to release chemicals into a soil environment to reduce soil pathogens. This study was focused on determining the effect of the pathogen on the growing biofumigant plants and the subsequent incorporation into the substrate. Various cultivars of mustard, wheat, and peas were grown in a controlled setting and inoculated with a pathogenic Pythium spp. Disease ratings were then calculated on the corresponding stands. Properly prepared mustard residues were then put into the system to see if an effect could be obtained. Microbial soil counts were then performed to determine if a biofumigant effect occurred.

16A-U. Effect of Ammonium Salt on Root Nodulation in Legumes in Hydroponic Settings. <u>Jack Outlaw</u>, Levi Mounce, Amber Lancaster, and Gary Bates. *Biology Department, Northwest Arkansas Community College, Bentonville, AR 72712.*

Growing plants in hydroponic settings has becoming more popular due to its ability to quickly produce a crop in limited space. Since these systems are artificial it is difficult to maintain a balanced fertilization regiment. Imbalance in the system is known to cause problems in crop yield and quality. Furthermore, it is unknown what role symbiotic rhizosphere microbes play in this system. The effects of beneficial microbes on plant growth are unknown in a hydroponic system. Legume plants are well known for living in a symbiotic relationship with nitrogen fixing bacteria. This study focused on a hydroponic system and the interactions of fertilizer and root nodulation in the presence of nitrogen fixing bacteria.

16B-U. Microrna **181-a/-b** Can Target Integrin Alpha1 in Lung Cancer. Julius B. Danquah and Xiaochao Tan. Biology Department, Philander Smith College, Little Rock, AR 72202.

Integrins have been found to play key roles in the regulation of cellular behavior such as proliferation and survival, upon activation by binding to extracellular matrix components. Their implication in the proliferation, survival and migration of tumor cells has made them an appealing target for cancer therapy. During our studies about integrin alpha1 subunit (a transmembrane receptor for collagen in the cell matrix) which mostly has aberrant expression in lung cancers, we found that the 3' UTR of this receptor has intriguing complementaries to the seed sequence of members of the microRNA 181 family (small noncoding RNAs that regulate gene expression activities) suggesting that integrin alpha1 may have a potential binding site for this family of noncoding RNAs. By using luciferase and GFP reporter assays, we found that microRNA 181-a/-b can directly target the 3' UTR of integrin alpha1. Simply, we inserted the 3'UTR integrin alpha1 downstream the luciferase reporter gene and used together with miRNA 181 in co-transfection using murine cells. Expression of the 3'UTR was determined by assessing the enzymatic activity of the reporter gene which was markedly reduced when microRNA 181 was present. This finding indicates that microRNA 181-a/-b may down-regulate the expression level of integrin alpha1 in tumor cells and may be a promising therapeutic target for lung cancer.

17A. Bacterial Diversity of an Abandoned Mine Land in SE Kansas. <u>Rachel Bechtold</u> and Anuradha Ghosh. Biology Department, Pittsburg State University, Pittsburg, KS 66762. Acid mine drainage (AMD) is found in areas of abandoned coal mines in Southeast Kansas as a result of mine waste runoff. AMD lowers the pH of groundwater, creating problems for both flora and fauna in the vicinity. Soil bacterial population acts as a reliable indicator of health of an ecosystem, especially in human-perturbed regions. The goal of the present study was to assess the temporal bacterial diversity of AMD sites over a two-year period and attempt to isolate acidtolerant bacterial species that could be employed back into the site for bioremediation purpose. In fall (2015), soil samples were aseptically collected from five distant sites representing diverse topography. Soil texture was evaluated and subjected to biogeochemical analysis. Samples were dilution plated on tryptic soy agar, concentration of bacterial isolates were determined by counting CFUs. Up to thirty morphologically different colonies were identified using physiological and biochemical tests. Preliminary data obtained in this study showed that soil pH ranges from 2.5 to 6.8. Other biogeochemical analysis data are expected. The concentration of bacteria varied on various samples: range 2x10^5 - 0.5x10^2 CFU/g of soil. A total of 7, 5, 8, 3, and 7 selected isolates from 5 sites, respectively, are being identified following biochemical tests. Their identity would be further confirmed by 16S rRNA gene sequence analysis. Future samplings would be done this summer (2016). A baseline measurement of bacterial diversity, as well as soil chemistry of AMD sites in this region, is novel in its kind and the findings could be used for future remediation of contaminated AMD sites.

17B-U. Three Year Comparison Study of Total, Fecal, and E. coli Coliform Concentrations in Lake Columbia and the Effects of Environmental Factors on Their Growth. <u>Kara O'Neal</u>. Chemistry and Biochemistry, Southern Arkansas University, Magnolia, AR 71753.

Total coliform bacteria are natural indicators of pollution in fresh water sources such as lakes, ponds, and streams. The presence of fecal coliforms, a subset of total coliforms, means there is a potential for viable pathogenic organisms in a water source. Escherichia coli (E. coli) coliforms are a subset within fecal coliforms. Some strains of E. coli are nonpathogenic while other strains such as O157:H7 are pathogenic and can cause gastrointestinal issues. The monitoring of these coliforms is essential to determining whether water sources are contaminated. In this study, weekly samples were collected from the Southshore Landing at Lake Columbia in Magnolia, Arkansas. Samples were tested for enumeration of total, fecal, and E. coli coliforms. Environmental factors that had the potential to affect coliform growth were also monitored weekly in order to determine whether there was a direct correlation between the two. These parameters included: conductivity, dissolved oxygen, pH, temperature, and turbidity. Analysis of the collected

data revealed that there were correlations between environmental factors and coliform growth.

18B-U. Characterizing the Maintenance Role of MLL1 in Human Acute Myeloid Leukemia. <u>Donnell White</u> and Patricia Ernst. *Natural Science Department, UA Monticello, Monticello, AR* 71655.

A prominent characteristic of leukemia in infants is a high frequency of chromosomal translocations affecting the endogenous MLL1 (or KMT2A) gene at 11q23, resulting in a MLL1 fusion protein. Controversy regarding the role of endogenous MLL1 in MLL-fusion leukemia resulted in our lab demonstrating with murine model systems that MLL1 is not necessary for MLL-AF9 driven acute myeloid leukemia (AML). To test the hypothesis that this is also true of human AML, a CRISPR-Cas9 system was developed to remove MLL1 from a human MLL-AF9 leukemia line. The cell surface protein CD38 was used as a positive control to establish a stable CRISPR-Cas9 system. Reduced CD38 in targeted AML cells is expected. The established CRISPR-Cas9 system could introduce mutations into the endogenous human MLL1 gene, and the growth of these cells assessed to determine the role of endogenous MLL1 in leukemogenesis. A human AML cell line expressing Cas9 was produced by lentiviral-Cas9-GFP transduction into the Molm13 (MLL-AF9) leukemia line. GFP+ cells were sorted and expanded, and flow cytometry and western blotting assay was used to confirm Cas9 expression. A high titer lentivirus was needed to deliver guides for CD38, KMT2A, and a negative control non-targeting sgRNA into the Molm13-Cas9 cells. Fugene6 was used to create the virus. Three trials were conducted in an effort to optimize and obtain high Fugene6 tranfection efficiency. Due to low virus titer using Fugene6, a calcium phosphate tranfection method was tested, and the virus was produced using this method. Molm13-Cas9 cells were infected with lenti-CD38 virus, and infection efficiency was determined using flow cytometry. An additional system is being developed in which Cas9 nuclease and sgRNA are introduced into AML through the same vector. Infection using the single vector system is ongoing.0.8% of the Molm13 cells initially infected expressed GFP. Seven days post sorting, 84.1% of the cultured cells were GFP+. Western blotting confirmed Cas9 protein expression. After a month, GFP+ cells were reduced to ~50%. For producing guide expressing lentivirus, transfection efficiencies using Fugene6 were ~39%. Multiple transfection trials for CD38, KMT2A, and non-targeting sgRNA plasmids yielded similarly low efficiencies, thus prompting us to test calcium phosphate transfection, which yielded >97% transfection efficiencies. Despite these higher transfection efficiencies, low titer virus was produced, leading us to swap viral packaging components to identify suboptimal reagents. Nonetheless, our trial using this low titer virus suggested that CD38 reduction

was achieved in a low percentage of cells. We optimized conditions for making lentivirus in our lab but need to further optimize production of high titer lentivirus. While performing these studies, several lentiviral systems were considered for introducing both guide RNAs and Cas9. Our studies suggest that CD38 has potential as a suitable positive control to test our system's efficiency. Optimizing viral titer is essential for moving on to more challenging targets, including the nuclear MLL1 protein. With a higher titer lentivirus and potential changes in the lentiviral system used, mutations in human endogenous MLL1 will be effectively introduced, resulting in an AML cell line without MLL1. The maintenance role of endogenous MLL1 in human AML can then be determined.

19A-U. Does exposure to different concentrations of caffeine affect Dictyostelium development? Sanhya Baviskar, Loi Bui, and Allyson Frantzen. Cell and Molecular, UA Fort Smith, Fort Smith, AR 72904.

The soil amoeba, Dictyostelium discoideum, has been one of the most popular model organisms in molecular biology. Due to its simple life cycle, small genome size, and availability, it is used to conduct experiments in cell and molecular biology and developmental biology. Caffeine is the world's most widely used psychoactive drug that stimulates the central nervous system. It can alter the physiology, mood, and behaviors of our body. The goal of this project is to observe how caffeine affects Dictyostelium development. Dictyostelium cells would be allowed to undergo development by placing them on starvation plates with different caffeine concentrations. Dictyostelium development would be observed at different time points during development and compared with the control starvation plates. Based on preliminary data, we hypothesize that higher concentrations of caffeine would inhibit Dictyostelium development.

19B. Effects of Small Molecules on Protein Aggregation and Paralysis in C. Elegans Expressing Aβ1-42 in Muscle. <u>Samuel Kakraba</u>, Narsimha R. Penthala, Peter A. Crooks, Robert J. Shmookler Reis, and Srinivas Ayyadevara. *Bioinformatics, UA Little Rock, Little Rock, AR 72204 and UAMS, Little Rock, AR 72205.*

Abstract Background: Proteins require correct folding in order to function effectively and efficiently. Neurological disorders, such as Alzheimer's and Parkinson's diseases, and possibly a wide range of other age-associated diseases, are attributable to protein aggregation that is cytotoxic, especially to nerve cells. Our goal is to learn whether anti-inflammatory compounds are effective at reducing protein aggregation as well as preventing paralysis in C. elegans. Methods: Transgenic C. elegans which expresses human Aβ1–42 transgene in body-wall muscle shows ageassociated paralysis. In addition to conducting studies on a range of compounds as a first step in an iterative process of drug optimization, we have also tested doseresponse functions for the compounds in reducing protein aggregates in these strains. Results: Ageassociated protein aggregation is higher in untreated controls compared to compounds tested, suggesting that these anti-inflammatory compounds relieve protein aggregation and prevent age-associated paralysis. Discussion and Conclusion: These results have begun to provide a basis for considering the use of some of these anti-inflammatory compounds and their derivatives as novel therapy for protein aggregation disorders. Further studies are needed to understand the mechanisms by which these effects are observed and yield a potential use for these compounds as pharmacological interventions. Acknowledgement This project was made possible by a grant from the Life Extension Foundation, and the Arkansas INBRE program -supported by funding from the National Institutes of Health (NIH) National Institute of General Medical Sciences (NIGMS) (P20 GM103429) (formerly P20 RR016460).

20A. Oct4 and Nanog MRNA Upregulation in Human Foreskin Fibroblast with Short Telomeres. <u>Ethan M.</u> <u>Clement</u> and Calin O. Marian. *Biology Department, University of Central Arkansas, Conway, AR* 72035.

Cellular senescence denotes the biological aging of the cell due in part to the shortening of telomeres. In somatic cells, during normal chromosomal replication, the lagging DNA strand is not continuously replicated like the leading strand. This phenomenon, known as the end replication problem, leads to gradual telomere shortening after each cell division. In some normal actively proliferating tissues (such as skin, gut lining, hair follicle, etc.) as well as majority of cancer cells the end replication problem is solved by telomerase, a specialized enzyme that has the capacity to add telomere repeats to the end of chromosomes. Telomerase has two components, the RNA template (hTR) and the reverse transcriptase (hTERT). The reactivation of telomerase has been widely regarded as playing a vital role in the immortality of cancerous cells. Recently, telomerase inhibitor drugs have been shown to induce critical telomere shortening in various cancer types. Our major interest is to investigate the impact of these critically short telomeres on cancer cell and human foreskin fibroblast functions, specifically on selfrenewal pathways mediated by OCT4 and NANOG transcription factors. Validation of OCT4/NANOG upregulation during crisis in somatic fibroblast can provide insight into these self-renewal pathways. Preliminary RT-PCR data suggests mRNA from OCT4 and NANOG are upregulated in older fibroblast that express perinuclear ß-galactosidase as opposed to young fibroblast with smaller senescent populations.

20B-U. Blood Platelet Glycoprotein VI and the Progression of Sepsis. <u>Rachel Knight</u> and Jerry Ware. *Physiology Deparment, UA Monticello, Monticello, AR 71655; UAMS, Little Rock, AR 72205.*

Sepsis is a worldwide problem in medical management and in the U.S. accounts for 250,000 deaths annually, ranking it in the top 10 causes of death. The dynamic interplay between platelets, thrombosis, and inflammation presents major challenges to understanding the initiation and progression of sepsis. Determining specific in vivo platelet contributions to sepsis has been difficult owing, in part, to whether outcomes result from the platelet's role as an immune modulator. Our lab's previous data have established the platelet membrane receptor, termed glycoprotein (GP) VI, contributes to the platelet-dependent proinflammatory phenotype. Moreover, the human GPVI gene has 2 common haplotypes, designated GP6a and GP6b, with gene frequencies of 85% and 15%, respectively. We propose to test the hypothesis that human glycoprotein VI haplotypes influence the progression of sepsis. Approximately 60-120 blood samples from the Pediatric Intensive Care Unit (PICU) at Arkansas Children's Hospital (ACH) have been collected. Genomic DNA from each sample has been isolated and polymerase chain reaction (PCR) conditions established to determine the GCVI genotypes. The samples were obtained after Institutional Review Board (IRB) approval from the patients at various points along the clinical spectrum of sepsis. In brief, oligonucleotides have been designed and tested in the PCR to determine whether they can amplify the corresponding region of the human GPVI gene. Analysis of the PCR in DNA agarose gels and optimized purification strategies for the final DNA sequence analysis has been completed. Preliminary DNA sequence data confirms the sequence of the human GPVI gene and completion of the genotype assignments are underway. Ongoing correlation of the platelet GPVI haplotypes to the clinical presentation of the sepsis syndrome will complete the testing of our hypothesis.

21A-U. Regulation of Laforin Levels in Neurons Affected by Alzheimer's Disease. Maria Alejandra Zeballos, Saeed Y. Aghdam, Steve W. Barger. Biomedical Engineering, University of Arkansas, Fayetteville, AR 72701; UAMS, Little Rock, AR 72205.

Type 2 diabetes mellitus (T2DM) is a risk factor for Alzheimer's disease (AD). However, the pathway that links both diseases is undefined. T2DM generally involves abnormal regulation of glucose transport, including deficiencies in glucose uptake by the brain. In the brain, neurons are programmed to inhibit glycogen synthesis through their expression of a regulatory protein termed laforin. When this system malfunctions, e.g. when the laforin gene is mutated, the result is toxicity for the neurons. In previous studies, our group has found that laforin levels in brains with AD were reduced to almost half relative to laforin levels in normal brains. Furthermore, laforin interacts not only with enzymes that are involved in tau protein hyperphosphorylation, but also with tau protein itself. Abnormally phosphorylated tau protein forms neurofibrillary tangles (NFTs), which are a neuropathological feature of AD. The laforin gene promoter contains sequences that can be bound by the transcription factor termed hypoxia-inducible factor (HIF). HIF regulates the transcription of enzymes involved in glucose metabolism and its levels are downregulated in AD brains. Together, these findings suggest that some of the neuropathology occurring in AD may arise from the drop in the levels of HIF-1 α , a key subunit of the HIF complex; this may thereby diminish laforin levels. To test this hypothesis, we have begun to characterize HIF-1 α expression in a transgenic mouse model of AD and tested laforin regulation in human neuronal cells. We found that (1) the primary pyramidal cells of the hippocampus express substantial levels of HIF-1 α in the basal state, (2) modulators of HIF-1 α levels affected laforin transcription, and (3) a treatment aimed at reducing laforin levels elevated levels of hyperphosphorylated tau. These findings suggest a potential pathway by which T2DM and AD are linked. Determining a pathway linking both diseases is crucial to understand AD and to find a treatment.

21B-U. AMAP1 Affects Cetuximab Sensitivity by Regulating the Nuclear Localization of the Epidermal Growth Factor Receptor. <u>Antonio Igbokidi</u>, Haley Feezell, Jodi Simeon, Brook McGinness, and Tameka A. Bailey. *Biological Sciences, University of Arkansas, Fayetteville, AR* 72701.

Epidermal growth factor receptor (EGFR) positive, triple negative breast cancer (TNBC) is the most lethal form of breast cancer. Previous studies have shown that cextuximab, a humanized anti-EGFR antibody, abolishes signal transduction from cell surface EGFR but not nuclear EGFR. Consequently, as described by Li et al 2009, nuclear EGFR is a determinant of cetuximab resistance. Previous studies have shown that AMAP1 is a modulator of the ligand-dependent endocytic recycling of cell surface EGFR. However, it is unknown whether AMAP1 plays a role in the nuclear localization of EGFR. Here, we investigated whether AMAP1 impacts the nuclear localization of EGFR and consequently cetuximab sensitivity. If AMAP1 regulates the trafficking of EGFR from the cell surface to the nucleus, then inhibition of AMAP1 should increase cell surface EGFR and cetuximab sensitivity in TNBC cells.

22A-U. Rapid plasticity in human motor cortex following temporary digit fusion. <u>Megan M. Gardner</u>, Matthew A. Gannon, Stephanie M. Long, and Nathan A.

Parks. Psychological Science, University of Arkansas, Fayetteville, AR 72701.

Extensive literature has delineated remarkable effects of long-term neuroplasticity (weeks, months, or years) and topographical reorganization in sensorimotor cortex following amputation, stroke, and practice. However, very little is understood about the occurrence of early rapid functional adaptations in motor cortex representations that may mediate long-term reorganization. We investigated such short-term motor plasticity (minutes to hours) in human motor cortex by using event-related cortical motor event-related potentials (ERPs) in a temporary "digit fusion" paradigm. The index and middle fingers of the dominant hand were temporarily fused together with an over-thecounter topical skin adhesive. Such artificial syndactyly caused the two fused digits to move together as a single unit with use of the dominant hand. Immediately following digit fusion, we recorded motor ERPs in a simple bimanual motor response task and again approximately 45 minutes later, following a period of motor dexterity practice during which a set of fine motor tasks (Purdue peg board and marble parceling task) were repeatedly performed with the dominant and non-dominant hand. Motor potentials were also recorded in an additional control session in which subjects performed an identical set of tasks but without temporary digit fusion. Preliminary results indicate that, following practice with the fused digits, motor potentials increase in amplitude relative to the control session (or motor potentials evoked by responses given with the non-fused hand). These findings demonstrate the occurrence of rapid early functional adaptations in motor cortex following constrained motor output and are consistent with the occurrence of a mechanism of disinhibition within sensorimotor digit representations in driving such short-term motor plasticity.

22B-U. Distribution and Abundance of Introduced Seal Salamanders (Desmognathus monticola) in Northwest Arkansas, USA. <u>Clint L. Bush</u>, Jacquelyn C. Guzy, Kelly M. Halloran, Meredith C. Swartwout, Chelsea S. Kross, and John D. Willson. *Biological Sciences, University of Arkansas, Fayetteville, AR* 72701.

Many reptiles and amphibians are gaining recognition as harmful invaders, highlighted by well-known examples such as the brown treesnake (Boiga irregularis), cane toad (Rhinella marina), American bullfrog (Lithobates catesbeianus), and Burmese python (Python molurus bivittatus). In 2003, an introduced population of Seal Salamanders (Desmognathus monticola), was found in Spavinaw Creek, within the Ozark Plateau of Northwest Arkansas. Genetic evidence confirmed an introduction from northern Georgia. Very little is known about the status of this non-native population, thus, the objective of this study was to assess the current distribution and abundance of non-native D. monticola along Spavinaw Creek. We conducted repeated, low intensity visual surveys along the 30 km extent of Spavinaw Creek in Arkansas and used a hierarchical Bayesian analysis to model the occupancy response of D. monticola and five native salamander species relative to river mile and habitat covariates. We also conducted a short-term closed capture-mark-recapture study to estimate abundance of D. monticola at the original collection site on Spavinaw Creek. We found a clear geographic pattern of D. monticola distribution, with individuals found throughout the upper 10 km of Spavinaw Creek headwaters, but no clear habitat associations. Estimated abundance of D. monticola was extremely high - 14.5 individuals and 50 g wet biomass per square meter. Our results reveal that introduced D. monticola are much more widely distributed than previously recognized and occur at high densities, suggesting that this recent invader could negatively affect ecosystems of Spavinaw Creek and surrounding watersheds in the Ozark highlands.

23A-U. Functions of Lipin in the endocrine system of Drosophila melanogaster. <u>Emily Overman</u>, Stephanie E. Greene, Michael Lehmann. *Biological Sciences, University of Arkansas, Fayetteville, AR* 72701.

Lipin is a protein that dually acts as a phosphatidic acid phosphatase (PAP) and a transcriptional regulator. In both mammals and the fruit fly, Drosophila melanogaster, Lipin is required in fat tissue for fat storage. Interestingly, in fly larvae it is also expressed in the ring gland, an endocrine gland that produces the steroid hormone ecdysone. The active form of this hormone controls molts between larval stages and metamorphosis of the larva into the adult fly. Expression of a form of Lipin in the ring gland that lacks a nuclear localization sequence (LipinΔNLS) leads to a strong delay of development. This suggests that Lipin has a nuclear role in the synthesis of ecdysone and, therefore, normal development. However, expression of this form in the ring gland also causes an increase in PAP activity that results in the formation of large fat droplets. These droplets may trap cholesterol, the precursor for steroid hormone synthesis, which may in turn cause the observed developmental delay. The goal of the project is to test the two competing hypotheses, delay caused by loss of nuclear Lipin or delay caused by entrapment of cholesterol, by carrying out feeding experiments with cholesterol and ecdysone. If cholesterol does attenuate, or "rescue," the developmental delay, it will support the entrapment hypothesis. However, if feeding cholesterol does not rescue the delay, but feeding of ecdysone does, it would support the hypothesis that Lipin has a function in the nucleus that is required for normal hormone production.

23B-U. Molecular Dynamics Simulations of Peptide Binding/Insertion by Membrane Protein YidC. <u>Thomas</u> <u>Harkey</u> and Jeevapani Hettige. *Chemistry Department, University of Arkansas, Fayetteville, AR* 72701.

Newly synthesized membrane proteins must be accurately folded and integrated into the plasma membrane co-translationally. YidC is a universally conserved protein that mediates this process either individually as a membrane insertase or as a chaperone in the SecY complex. We are primarily concerned with the mechanism of substrate binding and insertion in the Sec-independent pathway. Structural studies have shown that the protein consists of five transmembrane helices that form a positively charged hydrophilic groove that is open toward both the lipid bilayer and cytoplasm, but closed on the extracellular side (Kumazaki et al., Nature 509:516, 2014). The proposed mechanism of the insertion involves the interaction between the highly active C1 region of the protein and the substrate protein. Despite much progress in determining the structure of YidC, many mechanistic questions remain unanswered. Our all-atom molecular dynamics (MD) simulations of membrane-embedded YidC can shed light on the binding/insertion mechanism of YidC at a detailed molecular level. The original crystal structure of YidC has a missing inter-helical loop from residues 195-216 in the C2 region. This loop is close to the functionally important and highly fluctuating C1 region. In order to study the peptide insertion mechanism, we first need to determine whether or not the missing loop plays any role in the binding and/or insertion mechanism. The simulations can be carried out both with and without the loop. We have thus systematically examined the influence of the missing C2 loop on the conformation al dynamics of the protein. We made two systems: one without the loop and one with a modeled loop. The final simulation systems consisted of about 62,000 atoms (in each case) including the protein, the lipid bilayer, and the water molecules as well as ions. Each system was simulated for at least 200 nanoseconds. The analysis of the resulting MD trajectories supported the hypothesis that the presence of the C2 loop stabilizes the protein, particularly in the C1 region, which is known to play an important role in the insertion mechanism. Based on these equilibrated systems, we can now perform a set of non equilibrium pulling simulations to induce the transition associated with the substrate binding and insertion mechanism.

24A-U. Creation and characterization of Lipin S147 mutants. <u>Austin Morgan</u>, Stephanie E. Greene, and Michael Lehmann. *Biological Sciences, University of Arkansas, Fayetteville, AR* 72701.

Lipins are proteins required for normal fat storage and adipose tissue development in various organisms. Lipins

function as phosphatidate phosphatases, which convert phosphatidic acid into diacylglycerol (DAG). DAG in turn is the direct precursor to triacylglycerol, which is the fat storage molecule found in adipose tissue. Apart from this enzymatic function, lipins can also stimulate the transcription of certain genes as transcriptional coregulators in the nucleus. The functionality of lipins is controlled by intracellular localization, which is in turn controlled by post-translational modifications, in particular, phosphorylations. Because humans have three different lipin genes, we use the single Lipin homolog of Drosophila melanogaster as a model in our studies. Lipin possesses a predicted phosphorylation site for the insulin-controlled protein kinase Akt at amino acid position S147. The objective of the project is to determine whether mutations of S147 have effects on the normal functions of Lipin. Using the CRISPR/Cas9 system, we introduced mutations into the Lipin gene that led to an exchange of the serine at position 147 by the amino acid alanine or by glutamic acid. Alanine is non-phosphorylatable and glutamic acid acts as a phosphomimetic, simulating constitutive phosphorylation of \$147. By examining the phenotypes of the two mutants, we hope to establish what effect phosphorylations on S147 have on Drosophila development and metabolism.

24B-U. Interaction Between Drosophila Lipin and the Mitogen-Activated Protein Kinase Pathway. Edward Richard Moran, Stephanie E. Greene, and Michael Lehmann. Biological Sciences, University of Arkansas, Fayetteville, AR 72701.

Lipins are proteins required for normal fat storage and fat tissue development in animals. We use the single Lipin homolog of the fruit fly, Drosophila melanogaster, as a model for Lipin function. Drosophila Lipin has properties that are very similar to those of the three Lipin homologs found in humans and other mammals. In the biosynthetic pathway that produces storage fat (triacylglycerol or TAG), Lipin serves as the enzyme that converts phosphatidic acid into diacylglycerol, the direct precursor to TAG. However, Lipin can also activate genes as a transcriptional co-regulator. Whether Lipin functions in fat synthesis or in regulating genes in the nucleus is largely dependent on intracellular localization of the protein. This localization is regulated by protein modifications, in particular phosphorylation. While other pathways are known to interact with Lipin, it also contains predicted phosphorylation sites for mitogenactivated protein kinase (MAPK). Proteins of the MAPK family regulate a number of cellular processes including cell proliferation and differentiation. The aim of the project is to determine whether genetic interactions exist between Lipin and members of the MAPK pathway that support a model in which Lipin is regulated by MAPK-controlled phosphorylation. To this end, flies with genotypes are constructed that allow simultaneous or

individual reduction of Lipin and members of the MAPK pathway. If an interaction indeed exists, effects on fat tissue development, viability, and other traits that are caused by reduction of one component should be enhanced or suppressed by reduction of the other.

25A-U. Roles of ligand-receptor interactions in axon guidance decisions of robo3 in Drosophila embryonic CNS. <u>Abigail Carranza</u> and Tim Evans. *Biological Sciences, University of Arkansas, Fayetteville, AR* 72701.

During the development of the nervous system, neurons extend membrane processes known as axons to form connections with other cells. The axon is able to sense extracellular cues through axon guidance receptors in the Roundabout (Robo) family. Robo receptors are transmembrane proteins that regulate many axon guidance decisions including midline crossing of axons in the central nervous system (CNS). In Drosophila, robo3 is one of the three Robo receptors that display specific expression patterns in the embryonic CNS and binds to the repellent ligand Slit. The significance that Slit has on Robo3 for the formation of axon pathways in the intermediate region of the neuropile is unknown. To determine the effect of the removal of Slit binding would have on Robo3's ability to form axon pathways, we used a CRISPR/Cas9-based approach to replace the robo3 gene with a modified version that is unable to bind Slit. We disrupted the ligand-receptor interactions by deleting the Robo3 lg1 domain, which is essential for Slit binding. We constructed a robo3∆Ig1 donor plasmid and a corresponding guide RNA (gRNA) plasmid to target the robo3 gene and delete the sequence encoding the Ig1 domain. Drosophila flies expressing Cas9 were injected with the gRNA plasmid and robo3∆lg1 donor, and we recovered the modified allele by screening the injected flies' progeny via PCR. We collected embryos carrying the modified robo3∆lg1 allele and stained them with antibodies to label the longitudinal axon pathways. We compared these embryos with wild type and robo3 mutant embryos to determine whether Robo3∆Ig1 can act equivalently to Robo3 to promote longitudinal pathway formation.

25B-U. Ontogeny of osmoregulation during early stages of development in Japanese medaka. <u>Taylor</u> <u>Winn</u>, Mary Bossus, Saxyam Gautam, and Christian Tipsmark. *Biological Sciences, University of Arkansas, Fayetteville, AR* 72701.

Euryhaline teleosts maintain stable internal osmolarity despite changes in environmental salinity. To adapt to different salinities, these fish regulate the uptake and excretion of ions by adjusting the expression of claudin tight junction proteins, ion transporters and channels in the integument (embryo only), gill, kidney, and gut. The present study uses an emerging model species, the Japanese Medaka (Oryzias latipes), to observe where and when those osmoregulatory proteins are expressed during the ontogeny of the fish. Medaka were bred in fresh water tanks and their embryos were harvested at five different stages, concurrent with development of the major osmoregulatory organs. Real-time PCR analysis was conducted in order to compare the mRNA expression of osmoregulatory proteins (claudins, Na+/K+-ATPase, solute carriers, anionic CFTR channel) over time. Some genes were expressed within 2 days after fertilization (stage 24) and stayed relatively constant throughout development. Other genes were elevated just prior to hatching (stage 37-40), including those thought to be associated with kidney (cldn10b), gill (cldn10d, cldn10e, cldn27a, cldn28b, ncc2b, nhe3b) and gastrointestinal (cldn15 paralogs) development. Future research using immunohistochemistry will be important in determining localization of the proteins during development, and providing further insight into osmoregulation in medaka.

26A. Phytochemicals reduce colonization factors and transcription of virulence genes for the human foodborne pathogen, Campylobacter jejuni in chickens. Abhinav Upadhyay, Komala Arsi, Basanta R. Wagle, Indu Upadhyaya, Sandip Shresthan, Pam Blore, Annie Donoghue, Narayan Rath, and Dan J. Donoghue. *Poultry Science, University of Arkansas, Fayetteville, AR* 72701.

The foodborne pathogen Campylobacter is the leading cause of bacterial gastroenteritis in humans resulting in an estimated 96 million annual infections globally. In the United States, an estimated 800,000 cases of Campylobacteriosis occur each year largely due to consumption of contaminated poultry products. Poultry carcasses get contaminated during slaughter from chicken intestinal contents where the pathogen normally resides. Motility and attachment to intestinal epithelium are the two major factors responsible for Campylobacter colonization in chicken. Reducing the expression of aforementioned factors could potential reduce Campylobacter survival in chickens and risk of subsequent human infections. This study investigated the efficacy of sub-inhibitory concentrations (SICs, concentration not inhibiting bacterial growth) of three, generally regarded as safe (GRAS)-status phytochemicals (trans-cinnamaldehyde 0.01%, carvacrol 0.002%, eugenol 0.01%) in reducing the major colonization factors critical for survival of C. jejuni in chickens. In addition, the effect of the aforementioned phytochemicals on the expression of critical colonization genes was studied using real-time quantitative PCR. All experiments had duplicate samples and were replicated three times on three strains of C. jejuni. Data were analyzed using ANOVA with GraphPad ver. 6. Differences between the means were considered significantly different at P<0.05. All phytochemicals reduced C. jejuni motility, and adhesion to chicken primary enterocytes (P<0.05). Real-time PCR revealed

that majority of phytochemical treatments reduced the transcription of critical chicken colonization genes in C. jejuni by at least 2 fold as compared to controls (P<0.05). Results suggest that trans-cinnamaldehyde, carvacrol, and eugenol could potentially be used to control Campylobacter colonization in chickens and reduce the incidence of human foodborne illnesses.

26B. Genetic factors required for the interaction of Campylobacter jejuni with free-living amoebae. <u>Deepti</u> <u>P. Samarth</u> and Young Min Kwon. *Poultry Science*, University of Arkasnas, Fayetteville, AR 72701.

Genetic factors required for the interaction of Campylobacter jejuni with free-living amoebae Deepti P. Samarth, and Young Min Kwon Department of Poultry Science, University of Arkansas, Fayetteville, AR 72701 Free-living amoebae are gaining recognition as a potential environment reservoir of many intracellular pathogens including Campylobacter jejuni, which implies the possibility of complex molecular interactions between amoebae and Campylobacter. In the current work, we constructed 10 deletion mutants of C. jejuni 81-176 for the genes previously shown to be important for invasion and intracellular survival in mammalian host (motAB, ciaB, kpsE, virB11, cheY, flaAB, cstII, docB, sodB, and cadF), and determined their internalization and intracellular survival in comparison with wildtype C. jejuni strain 81-176 using Acanthamoeba castellani, an aquatic free-living amoeba ubiquitously present in water-supply. Modified gentamycin protection assay was used to investigate the internalization and intracellular survival. The survival percent after 3 hrs., the incubation time for internalization was significantly lower in all mutants tested as compared to wildtype (p<0.05) except ΔcstII. Also, survival percent after 24 hrs. incubation (following 3 hrs. internalization period) were also significantly lower for all mutants as compared to wildtype (p<0.05). For 3hr internalization period and survival after 24 hr, wildtype showed 1.718% ± 0.33 and 1.709% ± 0.09 respectively while the mutants having highest and lowest percent survival demonstrated after internalization period (3hr) were $\Delta cstII$ (1.33% ± 0.09) and $\Delta flaAB$ (0.11% ± 0.07) respectively and 24hr. incubation followed by 3hr internalization period were $\Delta docB$ (0.53% ± 0.15) and Δ kpsE (0.014% ± 0.006) respectively. The result of this study highlights the conserved mechanisms of C. jejuni internalization and survival between amoeba and mammalian hosts. A better understanding of the C. jejuni-amoeba interactions may lead to the development of effective strategies to reduce the persistence of C. jejuni in the environment through amoeba-mediated protection. Key words: Campylobacter jejuni, amoeba, internalization, intracellular survival, genetic factors.

27A. Locally delivered iloprost via microdialysis sampling modulates macrophage activation and monocyte chemotactic protein 1 production. <u>Kamel</u> <u>Alkhatib</u>, Tina M. Poseno, Jeannine M. Durdik, and Julie A. Stenken. *Chemistry Department, University of Arkansas, Fayetteville, AR* 72701.

Statement of Purpose: Modulating the macrophage response to implants is of significant interest as a means to promote improved biomaterial/tissue integration. Macrophages are highly versatile cells, existing in a continuum of activation states playing a key role in regulating the foreign body response[1]. Iloprost is an anti-inflammatory and anti-fibrotic drug[2]. This study aims to investigate the role of locally-delivered iloprost in altering the macrophage activation state[3]. Our hypothesis is that iloprost is an appropriate macrophage modulator aimed toward promoting improved tissue remodeling after implanting microdialysis sampling probes. The microdialysis sampling probe serves as both the implanted biomaterial as well as the means to both deliver modulators and collect cytokines. Macrophage phenotype surrounding the dialysis probes was assessed by the collected concentrations of CCL2 and the presence of CD163+ cells in the tissue surrounding the implant. Methods: Two microdialysis probes (CMA 20, 10 mm length, with 100 kDa MWCO polyethersulfone membranes, Harvard Apparatus, Holliston, MA) were implanted in the dorsal subcutaneous space of 5 male Sprague-Dawley rats (275-330) grams. One probe served as a control probe with 2% BSA in Ringer's solution (147 mM NaCl, 4.6 mM KCl, 2.3 mM CaCl2) as a perfusion fluid while the second probe was employed as a treatment probe delivering iloprost (1 pg/mL) in the same vehicle as with controls. After implantation, dialysates (1 hr collection) were collected daily for 4 hours to 2 days post implantation. After completion of the experiments, the rat was euthanized and the tissue surrounding the probes was excised for immunehistochemical and histological analyses. CCL2 concentrations were quantified in the dialysates using ELISA. Results: A combination of less cellular density and less collagen formation was observed in the tissues surrounding the iloprost-treated probes compared to the tissues around the control probes. Immunohistochemical analyses showed a greater number of CD163+ cells in the tissue around the treatment probe compared to the control probe. On the day of implantation CCL2 concentration in the dialysates ranged from 200 to 12,000 pg/mL in the control side, while it was between 250 and 6000 pg/mL in the treatment side. By the end of day 2 post implantation, CCL2 concentrations decreased from 5000 to 1800 pg/mL in the treatment side, while it was steady in the range of 5000-6500 pg/mL in controls. Conclusions: Iloprost has been used as a modulator to shift the macrophage phenotype. The localized delivery of iloprost leads to a decrease in concentration of proinflammatory chemokine (CCL2), less cellular density and less collagen formation which suggests the potential use of iloprost in modulating the foreign body response to an implanted biomaterial. References: [1] Porcheray F., Viaud S. et al. (2005) Clinical & Experimental Immunology 142, 481–489. [2] Gomez-Arroyo, J., Sakagami, M. et al (2015) European Respiratory Journal, 45(2), 449-462. [3] Murray, P. J., Allen, J. E., et al (2014). Immunity, 41(1), 14-20.

27B. In vivo structure-function analysis of Drosophila Robo1. <u>Haley Brown</u>, Marie Reichert, and Tim Evans. *Biological Sciences, University of Arkansas, Fayetteville, AR* 72701.

The repellant ligand Slit and its Roundabout (Robo) family receptors regulate many aspects of axon guidance in bilaterians, including midline crossing of axons during development of the embryonic CNS. Slit proteins are produced by midline cells and signal through Robo receptors expressed on the surface of axonal growth cones to repel axons from the midline. Disruption of Slit-Robo signaling causes ectopic midline crossing phenotypes in the CNS of a broad range of animals, including insects and vertebrates. Drosophila Robo1 has a conserved ectodomain structure of five immunoglobulin-like (Ig) domains plus three fibronectin (FN) repeats. We have previously shown that the Ig1 domain is essential for Robo1's midline repulsive activity in the Drosophila embryonic CNS. Here, we test the functional importance of each of Robo1's Ig and FN domains, by using a genomic rescue construct based on endogenous robo1 regulatory regions to restore expression of Robo1 Δ Ig1, Robo1 Δ Ig2, Robo1 Δ Ig3, Robo1 Δ Ig4, Robo1 Δ Ig5, Robo1 Δ FN1, Robo1 Δ FN2, Robo1ΔFN3 or Robo1ΔFN1-FN3 in embryonic neurons of robo1 mutants. We find that individually deleting any of the other four Ig domains (Ig2,3,4,5) or three FN repeats (FN1,2,3) does not impact Robo1's role in midline repulsion. Further, deletion of all three FN repeats together (Robo1∆FN1-FN3) does not disrupt Robo1's midline repulsive activity. We conclude that the Slit-binding Ig1 domain is the only immunoglobulin-like domain necessary for Robo1's midline repulsive role in an endogenous expression context in intact animals.

28A. Efficiency of the nuclease I-Scel in excising selectable marker genes from the plant genome. Elliott Pruett, Soumen Nandy, and Vibha Srivastava. Crop, Soil and Environmental Sciences, University of Arkansas, Fayetteville, AR 72701.

Gene stacking is a method used in biotechnology by which multiple genes can be placed at a single genomic site, thereby simplifying plant breeding. In this approach, DNA nucleases are used for excising selectable marker genes (SMG), which are the unneeded components of transgenic plants. The goal of this project is to evaluate the effectiveness of the nuclease I-SceI in excising DNA in plants. Specifically, this study tests heat-inducible I-SceI through the use of a heat-shock promoter (HS) in order to control SMG excision by heat application. The DNA plasmid containing a visual marker gene flanked by I-SceI target sites and the heat-inducible I-SceI gene has been created and confirmed. Arabidopsis thaliana plants have been transformed with the plasmid, which will be used for testing the efficiency of HS:I-SceI in excising DNA from plant genomes.

28B. Characterization of a Protein-Protein Interaction Involving the Ras-Related Protein Rheb and a Tuberous Sclerosis Complex 2 Variant. <u>Nosaiba Shokr</u> and Paul Adams. *Cell and Molecular Biology, University of Arkansas, Fayetteville, AR* 72701.

In order to understand the biological interactions, it is essential to relate the structures with the functions of any complex. Tumor suppressor complex 2, TSC2, plays a significant role in many pathways such as proteins synthesis, cell cycle, and signaling. Importantly, it acts as a GTPase activating partner for Ras homology enriched in brain, Rheb. It partially controls converting Rheb-GDP inactive form to Rheb-GTP active form through mammalian Target of Rapamycin, mTOR, pathway. Mutation in TSC2 causes abnormal activation of Rheb, but the molecular details of this interaction are still mysterious. We will study the effect of mutated TSC2 that may alter the catalytic activity of GTP hydrolysis or may weaken the protein complex formation. If the mutation in the adjacent binding domain to the GAP binding activity, it may stabilize the interaction of TSC2stimulated GAP activity, which will support if there is any difference in the orientation of the mutation.

29A. Bactericidal Nanofibers for Industrial & Biomedical Applications. <u>Parker Cole</u>. Mary Malloy, Jessica Paschal, Savannah Thornburgh, Franck Carbonero, and Z. Ryan Tian. *Food Science and Chemistry Departments, University of Arkansas, Fayetteville, AR* 72701.

Transmission of pathogens and resulting biofilm growth have gained increasing importance in industrial applications like water treatment and sanitation, food packaging, and public environments, such as public transportation. In addition, reports indicate that nosocomial infections account for 2 million infections and 90,000 preventable deaths per year in the US. Utilizing nanotechnology provides a good platform to alter physical-chemical properties of different materials compared to their bulk counterparts that can be harnessed for bio-applications. Several nanoparticles, such as silver, iron oxide (Fe3O4), titanium dioxide, zinc oxide (ZnO) and gold have been extensively studied for their antimicrobial activity. The drawback from using various nanomaterials is the lack of cost-effective methods to yield bactericidal composites for use in these niche applications. Herein, we are reporting biocompatible, anti-microbial nanomaterials via facile, cost-efficient methods for integration in biomedical and industrial applications. Our materials can be used for water treatment in cooling towers, bactericidal activity on orthopedic implants, and potentially reducing airborne infection through ventilation filters. In addition to this, our materials can be reused upon UV or WL cleaning or chemical washing which is a unique property to this disruptive product.

29B. Exploring Biogenesis of Iron-Sulfur Clusters in Methanogens. <u>Thomas Deere</u>, F.H. Lessner, E.C. Duin, and D.J. Lessner. *Cell and Molecular Biology, University of Arkansas, Fayetteville, AR* 72701.

Iron-sulfur (Fe-S) clusters are important prosthetic groups used by proteins involved in diverse processes essential to life, including photosynthesis, respiration, and DNA damage repair. Proteins utilizing Fe-S clusters are found in all three domains of life. Substantial evidence supports that cells have dedicated protein machinery for the synthesis, maintenance, and trafficking of Fe-S clusters (i.e. Fe-S cluster biogenesis). Fe-S cluster biogenesis has been studied extensively in bacteria and eukaryotes, revealing three systems (Nif, Isc, and Suf) with conserved features. Each system uses a cysteine desulfurase (e.g. IscS) to liberate sulfur from cysteine and deliver it to a scaffold protein (e.g. IscU). The Fe-S cluster is assembled on a scaffold and delivered to a target apo-protein. The genomes of anaerobes, particularly methanogenic archaea, code for the highest number of Fe-S cluster proteins. Moreover, central metabolism in methanogens is dependent on numerous Fe-S cluster proteins; yet very little is known about factors involved in Fe-S cluster synthesis in these cells. Bioinformatic analyses indicate core components of Isc and Suf systems are conserved in archaeal genomes. The Suf system appears nearly universal in archaea, with the Isc system often co-occurring. Interestingly, some methanogens appear to encode only Suf, lack a cysteine desulfurase, and use sulfide instead of cysteine as sulfur source for Fe-S clusters, indicating methanogens may use novel factors for Fe-S cluster biogenesis. We use Methanosarcina acetivorans as a model to elucidate the factors involved in Fe-S cluster biogenesis in methanogens. M. acetivorans can grow with multiple carbon sources, and use sulfide or cysteine as a sole sulfur source. M. acetivorans contains three Isc operons, each encoding a cysteine desulfurase (IscS1-3) and a scaffold (IscU1-3), plus two Suf operons encoding SufBC scaffolds. Biochemical studies reveal that Fe-S cluster content in M. acetivorans varies under different growth conditions, and that the Isc2 operon encodes a functional cysteine desulfurase and scaffold. Genetic studies indicate the Isc2 operon is not essential,

but is important for metabolism under certain growth conditions. Overall, our results indicate that M. acetivorans, and likely other archaea, contain functional core lsc systems for Fe-S cluster biogenesis.

30A. STEAM-H: Collaborate, Innovate, and Inspire Your Community. <u>Shilpa Iyer</u>, Jeannie Hull, Ralph Henry, and Raj. Rao. *Biological Sciences, University of Arkansas, Fayetteville, AR* 72701.

According to a 2015 report published by the 'Trust for America's Health and the Robert Wood Johnson Foundation', Arkansas has the highest adult obesity rate (35.9%) and fourth highest childhood obesity rate (18.0%) in the nation. Mitochondrial genome and bioenergetic dysfunction have been linked with energy deficiencies found in obesity, and obesity-related diseases (diabetes, hypertension, cardiovascular diseases). Many individuals in our communities are at high risk of developing these diseases; yet are unaware of it. An urgent cell-to-society integrative approach is required to inform our community about the importance of mitochondria and "bioenergetics" in our daily lives. Results from our past experiences have demonstrated the success of an integrative STEAM-H (Science, Technology, Engineering, Arts, Mathematics, Health) approach that bring together perspectives from multiple disciplines to communicate this important public health concern. We are in the process of assembling a hybrid team of UArk faculty and students from different units to collaborate and develop innovative educational toolkits for middle/high school students; and to increase awareness and inspire our community.

30B. The Functional and structural analysis of robo2 in axon guidance. LaFreda J. Howard and Timothy Evans. *Biological Sciences, University of Arkansas, Fayetteville, AR* 72701.

Roundabout (Robo) family proteins regulate many axon guidance decisions in the Drosophila embryonic central nervous system. Robo1 and Robo2 facilitate midline repulsion in response to Slit, while Robo2 and Robo3 define the lateral position of longitudinal axon pathways. In addition to these shared roles, Robo2 can also promote midline crossing of axons, an activity that is not shared by the other Drosophila Robos. Previous gain of function and genetic rescue studies suggest that the different roles of Robo2 are specified by individual immunoglobulin-like (Ig) domains within the receptor. Ig2 is required for Robo2's pro-crossing function, while Ig1 and Ig3 are thought to regulate lateral positioning. It has been assumed (but not directly demonstrated) that Robo2 acts as a canonical cell-autonomous Slit receptor to signal midline repulsion; if so, this activity would likely require the Slit-binding Ig1 domain of Robo2. We are using a CRISPR/Cas9-based gene replacement

approach to investigate which domains of Robo2 (Ig & Fn) are required for each of its axon guidance activities. By replacing the robo2 coding region with epitopetagged cDNAs, in which individual domains have been deleted, we are examining the contributions of each domain to receptor localization, regulation, and Robo2dependent axon guidance outcomes. We observed a mislocalization of protein when looking at Robo2 without its Ig1 domain. We are also currently examining the roles of the cytoplasmic domains of Robo2 with a similar approach. Our results promise to increase our understanding of how individual receptors can contribute to multiple axon guidance outcomes during developmental wiring of the nervous system.

31A-U. Cliff Swallows (Petrochelidon pyrrhonota) Prefer to Nest in the Center of Colonies. <u>Shelby</u> <u>Osborne</u>, Charles Ruiz, Steward Huang, and Ragupathy Kannan. *Biology Department, UA Fort Smith, Fort Smith, AR 72904.*

Predator avoidance is a major factor influencing nest site selection in birds. Cliff Swallows are common colonial nesting birds in summer in North America. They construct oblong mud nests mainly under bridges and overpasses. Old nests from previous years are frequently enhanced and reused. Previous studies have documented snake predation in these colonies, with nests located at the edge being more vulnerable to predation than those at the center of the colonies. We tested the hypothesis that Cliff Swallows prefer to nest more in the center of a colony than the edge. We predicted that if the hypothesis is true, then: 1. there will be more nests in the central compared to edge zones, 2. there will be more tiered or stacked nests in the central than in the edge zones, and, 3. central nests, due to frequent reuse, would have higher masses than edge nests. We conducted field work in the summer of 2016 at a bridge colony at Massard Road in Fort Smith, Arkansas (Sebastian County). All nests on both sides of the bridge were counted, removed, and weighed. The colonies were photographed before removal. The "center" of the colony was defined as the mid 50% of the length of the colony, and the "edge" was defined as 25% of the length on both sides of the colony. Our data strongly supported our hypothesis. All three of our predictions were met. There were more nests at the center (109) than the edge (86); there was just one set of 4 stacked nests at the edge compared to eight sets of 2-6 stacked nests in the center; and finally, central nests were heavier (572 gms±179 [259-1360]) than edge nests (511 gms±123 [246-830]) (mean, std., range). The difference in the masses was statistically significant (t = 2.69, P = 0.003, one-tailed t-test). Our study shows that Cliff Swallows have a clear preference to nest in the center of colonies.

31B-U. Eddystone Beacons: An application for Earthquake Survivors Identification. Jaylen Gregory, Vikram Sadhya, Jesse Allison, Gabriele Piccoli, and Dario Bonaretti. *Engineering and Information Technology, University of Arkansas at Little Rock, Little Rock, AR* 72204.

This dissertation examines the uses for Bluetooth beacons as well as applications used to better the devices' capabilities. Eddystone beacons are Bluetooth beacons that can be used to triangulate the position of survivors after an earthquake or other natural disaster. When in range a smartphone user can link to one or more beacons and a search crew will be able to see where they are within the structure. Earthquakes are becoming more prevalent today and the traditional method of digging through rubble without beacon technology can cause problems such as crushing a victim or even not getting to one in time. This tool offers an admirable alternative to search crews looking blindly through a building and can speed up the process significantly. Using HTML, Javascript and Node.js, our team created a webpage that becomes accessible as users with smart devices approach the beacons. For the experiment we would simulate an earthquake by having "survivors" scatter throughout a building and have one search crew that acted as the control group and another with beacon technology. We were not able to yet complete the experiment but for future work we would place about 25 beacons throughout a building and execute the experiment. Big picture we would like to have these beacons in places prone to earthquakes and other natural disasters.

32A. Identification of Features of Aging. <u>Thomas</u> <u>Hahn</u>, Fusheng Tang, Richard Segall, and Helen Benes. *Information Science, UA Little Rock, Little Rock, AR* 72204.

Aging is the biggest health concern accounting for most of the expenses in healthcare. Therefore, the aim of this research is to improve our understanding of the conserved mechanisms of aging in order to find ways to reverse its adverse consequences and delay or even prevent the onset of age degenerated diseases. We use time series data from yeast and maybe later also from other species to look for conserved changes in gene expression and protein expression patterns over time. A list of time series datasets for yeast can be found at http://microbialcell.com/table-1-hallmarks-of-humanaging-aging-in-yeast/ [1]. Pathway and Gene Ontology analyses are used to identify pathways, molecular functions, biological processes and cellular components that change in response to aging in a similar way. Emphasis is placed on understanding how the decoupling between transcription and translation drives the aging process [2]. Changes in the translational machinery, particularly affecting ribosomes and their

assembly are considered. Lifespan data from 674 knockout mutants [3], for which transcription and translation was measured at 12 different time points in the yeast's life [2], is used to find correlations between changes in the gene expression patterns associated with aging. Knocking out genes, for which the uncoupling between mRNA and protein abundance rises over time, tend to extend lifespan. Hence, we conclude that changes in the relationships between transcriptome and proteome over time need to be considered to quantify the contributions of different genes to the overall aging process. Gene Ontology Enrichment Analysis is performed for genes with similar aging related changes in gene and protein expression pattern and relationships between them in order to predict still unknown roles of other genes in the aging process. References: [1] Georges E. Janssens, Liesbeth M. Veenhoff (2016). Evidence for the hallmarks of human aging in replicatively aging yeast. Microbial Cell 3(7): 263-274. [2] Janssens, G. E., Meinema, A. C., González, J., Wolters, J. C., Schmidt, A., Guryev, V., ... Heinemann, M. (2015). Protein biogenesis machinery is a driver of replicative aging in yeast. eLife, 4, e08527. http://doi.org/10.7554/eLife.08527 [3] McCormick, Mark A. et al. A Comprehensive Analysis of Replicative Lifespan in 4,698 Single-Gene Deletion Strains Uncovers Conserved Mechanisms of Aging, Cell Metabolism, Volume 22, Issue 5, 895 - 906 (see http://www.ncbi.nlm.nih.gov/pubmed/26456335)

32B. An Investigation into the Antimicrobial Effects of Fixed Aluminum Oxide Nanostructures. <u>Azure</u> <u>Yarbrough</u>, Nawzat Saadi, Laylan Hassan, Tansel Karabacak, and John M. Bush. *Biology Department, UA Little Rock, Little Rock, AR 72204.*

Metals have been used to inhibit microbial growth for thousands of years; this effect is due to the oligodynamic effect. This antimicrobial phenomena is not completely understood; analysis of the current research suggests that the metals interact with either the thiol or amine groups found on both enzymes and proteins. Aluminum oxide (Al2O3) is one such metallic material that has been found to have antimicrobial activity, and it has been investigated using standard nanoparticles; two methods of action have been proposed for this. The first involves the presence of ionic and colossal structural patterns, which facilitates the interaction with or penetration of the cell membrane; the second method involves the possible uptake of the nanoparticles after interacting with the charged outer membrane and subsequent channel formation in the cytoplasmic membrane. Our group is interested in determining the bacteriostatic effect using fixed nanostructures of this metal, and if possible, the mechanism of this effect. We hypothesize that a similar effect will be found upon exposing bacteria to fixed Al2O3 nanostructures. In our present study, squares of

aluminum were treated with boiling double distilled water for various periods of time leading to the formation of Al2O3 nanostructures. These squares were then used in a variety of experiments to investigate their antimicrobial effects on E. coli. In a preliminary experiment, bacterial culture was placed on top of the samples, incubated at 37ºC, and samples were removed and plated at specific time points. We found that with an increase in the nanostructure formations of the metal on the squares, there was a corresponding decrease in bacterial growth; when the samples were used as stamps on nutrient agar plates, again, we found that there were fewer surviving colonies resulting from incubation with the metal samples with the highest levels of nanostructural formations Next, we used re-growth assays to test whether the decrease in growth was due to bacteriostatic or bactericidal effects. There was growth after each experiment which suggest that the nanostructures had a bacteriostatic effect instead of a bactericidal outcome. Finally, using the same metal samples in a modified Kirby-Bauer, we found that bacterial growth was inhibited directly under the metal; however, no zones of inhibition formed around the metal samples. The original hypothesis stands based on analysis of our current results, and we believe that the first mechanism, involving the ionic and colossal structural patterns, is responsible for the bacteriostatic effect of the nanostructures. The inhibition of microbial growth, ease and cost of manufacturing, and fixed nature of the nanostructures suggests these metal structures could be important for a variety of future bacteriostatic applications such as coating air ducts, food service areas, and medical equipment.

33A-U. Forensic Pathology: The Role of Body Decomposition & Determining Time of Death. <u>Sydnee</u> <u>Worlds</u> and Anissa Buckner. *Forensic Science, UA Pine Bluff, Pine Bluff, AR* 71601.

Body decomposition plays a huge role when it comes to determining the time of death. Unfortunately, there is relatively a lot more to be studied before scientists develop more secure ways of determining the post mortem interval or time since death. There are other methods that pathologists use to determine the time since death. By understanding the stages of decomposition such as algor mortis, livor mortis and rigor mortis, it can be determined when a person has died, although, there are other factors that must be considered such as body covering, body weight and the affect the environment can have on the body that could accelerate or inhibit the rate of decomposition ultimately effecting the estimated time of death. Other methods such as using body fluids, have given scientist more security when determining time of death due to the lesser amount of room for error. Entomology is another break through that scientist use to determine

time of death. By studying the life cycle of the blowfly and pinpointing the stage of development this information can be used to come to an accurate PMI.

33B-U. Earthworm Soil Preference. <u>Malachi Miller</u> and Steven Green. *Biology Department, UA Pine Bluff, Pine Bluff, AR* 71601.

People all over the world may know what an earthworm is, but many may not know the role earthworms play in the agriculture field. Earthworms help to increase the amount of air and water that gets into the soil, and when they eat, they leave behind castings that are a very valuable type of fertilizer for plants and soils. We hypothesized that earthworms have a preference for cover crops. Cover crops are crops planted in between regular crop seasons to prevent soil erosion. We wanted to determine which type of cover crops earthworms are more attracted to in order to help attract more worms and keep the soil healthy. We examined five different soil samples from different cover crop treatments: rye, hairy vetch, rape seed, a cover crop mix, and a chemically sprayed cover crop as a control. Using a Preference Chamber, the worms were placed in chambers, incubated, tallied through statistical analysis. Each test was repeated three times with ten worms each time. In conclusion, we determined that among cover crops: Rye > Vetch > Rape seed > Control was the earthworm's preference and the moisture content of the soil has an effect for earthworm preference.

34A-U. The Genetic Code: Pathways of the 20 Standard Amino Acids. <u>Annette Hall</u>, A.-M. Moorehead, and J. Onyilagha. *Biology Department, UA Pine Bluff, Pine Bluff, AR 71601.*

The origin of genetic coding is intriguing. From a pool of available molecules, life ended up using four nucleotides and twenty amino acids to encode and build its proteins. By the time of the Last Universal Common Ancestor (LUCA), the process of protein translation was largely fixed in the form of the standard genetic code. The intention of this research is to determine whether metabolic pathways found in living organisms are indeed an accurate guide to ancient evolutionary events. The project goal is to provide additional insight into the emergence of a standard alphabet of 20 genetically encoded amino acids. Consequently, we investigated the assertion that the 20 standard amino acids of the genetic code consist of early and late members, and that the late amino acids are "inventions" of early metabolism. In other words, genetic coding began with fewer than 20 amino acids. This "early" alphabet (comprising prebiotically plausible amino acids) was then augmented as metabolism evolved new possibilities, and incorporated them into genetic coding. Contemporary data from databases were used. Pathways to amino acid biosynthesis were

analyzed. The synquences of enzymes catalyzing the pathways were also studied. Our findings are consistent with earlier reports that the 20 amino acids of the standard genetic code comprise of two different groups: "early" amino acids that were likely available at the origin for life through prebiotic syntheses, and "late" amino acids that are best understood as inventions of biology itself. The results show that steps in the biosynthetic pathways of many of the late amino acids are longer than those of the early amino acids. Again, longer step means the involvement of many more enzymes. Additionally, late amino acid members are synthesized through several more pathways than the early amino acids. However, our results are at variance with some of the theories surrounding the evolution or emergence of the 20 encoded amino acids of the standard genetic code, especially the "precursorproduct" assertion of the "Co-Evolution theory". Firstly, the theory asserts that each new amino acid (product) is synthesized from a pre-existing precursor. For example, glutamine is synthesized from glutamic acid; tryptophan and cysteine are synthesized from serine. Secondly, the theory asserts that this relationship is reflected in the assignment of amino acids to codons within the genetic code. These assertions are inconsistent with our findings. For example, there is no precursor-product relationship that connects Glycine (Gly) and Threonine (Thr) amino acids as claimed by the Co-Evolutionary theory. In other words, Thr cannot be synthesized from Gly and vice-versa. Nevertheless, our results show new pathways that facilitate the biosyntheses of Thr from Gly and/or vice-versa. Consequently, we conclude that the origin of amino acids of the standard genetic code is far from being resolved and that there is need for a critical evaluation of the theories surrounding the emergence of the 20 standard amino acids. * This research was sponsored by the NSF/HBCU-UP program.

34B-U. Individualized, Programmable, Environmental-Triggered Delivery of Chemotherapeutics. <u>Madison</u> <u>Shaw</u>, Jordan Burkdoll, Heather Becker, Hannah Lowe, Oscar Chavez, Parker Cole, Asya Ozkizilcik, and Z. Ryan Tian. *Chemistry Department, University of Arkansas, Fayetteville, AR* 72701.

Drug delivery systems are engineered technologies for the targeted delivery and/or controlled release of therapeutic agents. Plentiful administration systems have been developed; however, after administration these drugs are typically delivered to the liver and metabolized [...] and subsequently transported in conjugated or unconjugated form to the diseased microenvironment. This method potentially leads to toxicity that can be circumvented with a controlled drug delivery system. Ideally, a controlled drug delivery system requires simultaneous consideration of several factors, such as the drug property, route of administration, nature of delivery vehicle, mechanism of drug release, ability of targeting, and biocompatibility. We are reporting a hollow-capsule vehicle with (i) a tunable void-volume for maximally loading drugs and (ii) a porous wall for time-programmable release of the drugs in response to external stimuli (temp. conc. pH, etc.). In a pilot study using methylene blue as a model drug, our mechanism reached (i) a ~99% drug loading efficiency and (ii) sustained and programmable releases over a 48-hour window in phosphate buffered saline at 37°C. Our ongoing work has shown great promise in developing a dynamic drug delivery system for both intravenous and oral administration. This proof of a truly versatile platform concept is believed to be unique in the drug-delivery field.

35A-U. Evolutionary conservation of axon guidance: regulation of midline crossing by Robo receptors. <u>Trent Daiber</u> and Tim Evans. *Biological Sciences, University of Arkansas, Fayetteville, AR* 72701.

Evolutionary conservation of axon guidance: regulation of midline crossing by Robo receptors. In animals with bilateral symmetry, coordination between the two sides of the body depends on proper connections being formed across the midline of the central nervous system (CNS). To achieve this, developing axons must choose whether or not to cross the midline. An evolutionarily conserved family of proteins known as the Roundabout (Robo) family regulate this decision in a broad range of animals including vertebrates, insects, and nematode worms. Robo receptors are expressed on axons and prevent them from crossing the midline in response to the repellant ligand Slit. Although Robo family members are present in each of these species, it is not known that their mechanisms function the same way. To directly compare the midline repulsive activity of Robo receptors from different animals, we are introducing Robo receptor genes from other species into Drosophila and determining whether they can substitute for Drosophila robo1 to regulate midline crossing of axons in the fly embryonic CNS. We are focusing on Robo genes from the nematode Caenorhabditis elegans (which has a single Robo receptor known as SAX-3) and the mouse Mus musculus (which has three Robo receptors known as mRobo1, mRobo2, and mRobo3). We have successfully transformed the C. elegans sax-3 gene into Drosophila embryos, and we find that SAX-3 can be properly expressed in fly neurons and localized to axons in the CNS, and can partially substitute for Drosophila Robo1 to mediate midline repulsion. In addition, we have constructed clones with combinations of receptor domains, specifically the ecto, cyto, and perimembranes, of the Robo1/Sax-3 chimeras to find which domains function for commissure distribution.

35B-U. Identifying Cancer Stem Cell Characteristics in Lung Cancer Cells Pre-Exposed to Hypoxia or Radiation. <u>Raisa Rasul</u>, Azemat Jamshihi-Parsian, Ruud P.M. Dings, and Robert J. Griffin. *Department of Biomedial Engineering, University of Arkansas, Fayetteville, AR* 72701; Department of Radiation Oncology, UAMS, Little Rock, AR 72205.

Despite being the leading cause of cancer related death world-wide, little improvement has been observed in lung cancer survival rate during the past 30 years. Resistance to therapy of lung cancer is thought to be caused by cancer stem cells (CSCs), a type of cancer cells which cause tumorigenesis and heterogeneous tumor cell populations. Here, the role of the regions of hypoxic tumor micro-environment is examined to determine whether pre-exposure to hypoxia induces or causes cells to maintain CSC properties. Three non-small cell lung cancer cell lines, parental, pre-exposed to radiation, and pre-exposed to hypoxia, were examined for cell viability, clonogenic potential, and sphere formation. Initial data indicates that after 24 hours in hypoxia, the viability of pre-exposed cell lines was about 15% larger than the parental cell line. Additionally, the clonogenic assay revealed about 40% greater surviving fraction of the pre-exposed cells cultivated in normoxia after 10 and 15 Gray radiation doses, suggesting a degree of resistance to radiation-therapy. These cell lines, in both 2D and 3D cultures, grew 1.5 times slower than the parental line, a characteristic observed in dormant CSCs, and exhibited an enhanced number of spheres, indicating metastatic potential of those cells. Our preliminary data suggests that tumors exposed to long-term hypoxia in the body or treated with radiotherapy multiple times may exhibit more CSC properties in comparison to unperturbed cells. Indicative protein markers for i) stem cells (i.e. CD133 or EpCam); ii) metastatic potential (i.e. MMP-1); and iii) hypoxia (i.e. HIF-1 α), are currently being analyzed by Flow cytometry and Western blotting to further validate and expand our analyses. This information could be exploited to develop treatments targeting the growth of CSCs and improve or create new therapies to treat cancer.

36A-U. Do estrogens play a role in the balance of conventional T-cells and regulatory T-cells? <u>Amanda</u> <u>Ederle</u> and Barbara Fuhrman. *Department of Biological Sciences, University of Arkansas, Fayetteville, AR* 72701; *Department of Epidemiology, UAMS, Little Rock, AR* 72205.

Regulatory T cells (Tregs) protect their host from autoimmune and inflammatory diseases by reducing immune activation and suppressing immune responses to auto-antigens. The suppressive actions of Tregs may promote breast cancer pathogenesis by allowing cancer cells to evade the host immune response. We hypothesize that variations in circulating Tregs will be associated with breast cancer risks in healthy women. In postmenopausal women, higher estrogen levels increase one's risk of breast cancer (Zhang et al. 2013).

Circulating estrogens have been correlated with expansion of circulating regulatory T cells in women (Polanczyk et al. 2004) and are thought to influence immune responses via membrane estrogen receptors (Schneider et al. 2014). The use of aromatase inhibitors to reduce systemic estrogens in breast cancer patients has been associated with a decline in Tregs in tumor tissues (Generali et al. 2009). No study has yet considered immune modulation as a potential mechanism by which estrogens may influence breast cancer risk. We seek to test for a role of estrogens in the development, proliferation, and/or plasticity of Tregs in healthy women by studying expression of the CREM-alpha receptor in CD4+ lymphocytes. CREMalpha is an estrogen membrane receptor modulator that has been associated with reduced circulating Tregs in the setting of autoimmune diseases such as lupus. We hypothesize that women with higher levels of CREMalpha will have lower circulating Tregs (Polanczyk et al. 2004). In order to test this hypothesis, we will develop a protocol for measurement of CREM-alpha on CD4+ lymphocytes and characterize this measure by describing its interindividual variation and reproducibility in samples from men, premenopausal women, and postmenopausal women. For application in population research studies, assays must have adequate through-put and excellent reliability. Our work will provide preliminary data to support future studies of estrogens and Tregs as potential causal factors in the etiology of breast cancer. References: Generali, D., G. Bates, A. Berruti, M. P. Brizzi, L. Campo, S. Bonardi, A. Bersiga, G. Allevi, M. Milani, S. Aguggini, L. Dogliotti, A. H. Banham, A. L. Harris, A. Bottini & S. B. Fox (2009) Immunomodulation of FOXP3+ regulatory T cells by the aromatase inhibitor letrozole in breast cancer patients. Clin Cancer Res, 15, 1046-51. Polanczyk, M. J., B. D. Carson, S. Subramanian, M. Afentoulis, A. A. Vandenbark, S. F. Ziegler & H. Offner (2004) Cutting edge: estrogen drives expansion of the CD4+CD25+ regulatory T cell compartment. Journal of Immunology (Baltimore, Md.: 1950), 173, 2227-2230. Schneider, A. E., E. Karpati, K. Schuszter, E. A. Toth, E. Kiss, M. Kulcsar, G. Laszlo & J. Matko (2014) A dynamic network of estrogen receptors in murine lymphocytes: fine-tuning the immune response. J Leukoc Biol, 96, 857-72. Zhang, X. H., S. S. Tworoger, A. H. Eliassen & S. E. Hankinson (2013) Postmenopausal plasma sex hormone levels and breast cancer risk over 20 years of follow-up. Breast Cancer Research and Treatment, 137, 883-892.

36B-U. Effects of Short-term Oral Metformin on **Tumor Biomarkers in Endometrial Carcinoma.** <u>Dustin</u> <u>Brown</u>, Yanquing Yang, Alexander F. Burnett, Lorenzo Fernandes, and Rosalia C.M. Simmen. *Physiology and Biophysics, UA Little Rock, Little Rock, AR* 72204; UAMS, *Little Rock, AR* 72205.

The anti-diabetic drug metformin (1,1-dimethylbiguanide hydrochloride; MET) has recently attracted interest due to its anti-metastatic effects in pre-clinical studies and its potential to decrease risk of cancer occurrence in patients with diabetes. However, the effects of MET in obese, non-diabetic women with endometrial cancer remains unknown. In this randomized pilot study, we sought to investigate the pre-surgical effects of short-term oral MET on biomarkers of tumor growth. Obese (BMI≥30) nondiabetic women diagnosed with grade 1-2 adenocarcinoma of the endometrium and consenting to the study were randomly assigned to receive 500 mg oral MET twice a day for 14 days, followed by 850 mg oral MET twice a day for 14 days or no drug during the pre-surgical window between diagnosis and hysterectomy. Endometrial tumors were obtained at surgery and processed for immunohistochemistry. Fixed tumor tissues were analyzed for cellular markers of proliferation (Ki67) and apoptosis (TUNEL), and for expression of estrogen receptor alpha (ERa), progesterone receptor (PR), and tumor suppressors PTEN and Krüppel-like factor 9 (KLF9) in tumor epithelial and stromal cells. Four MET-treated and four untreated patients, matched for age and BMI, completed the study to date. MET treatment was associated with higher PR, and KLF9 and lower ERa immunoreactivities in glandular epithelial cells. MET treatment also was associated with higher PTEN immunoreactivities in stromal epithelial cells. There were no significant effects of MET treatment for Ki67 and TUNEL. Short-term MET treatment is associated with increased expression of anti-tumor markers in tumor epithelial cells of nondiabetic obese women with endometrial cancer. While more patients will be required to definitively evaluate the clinical relevance of these initial findings, the cellular changes are consistent with the anti-cancer actions of MET, independent of its anti-diabetic effects.

37A-U. Evaluating the effect of estrogen receptor inhibition on TMEM165 expression in breast cancer cell lines. <u>Shelby Sorrells</u>, Karen Abbott, and Blake Johnson. *Chemistry and Molecular Biology, Harding University, Searcy, AR 72143; University of Arkansas for Medical Sciences, Little Rock, AR 72205.*

In estrogen-receptor positive breast cancers, estrogen aids in cell and tumor growth. These breast cancers are usually treated using hormone therapy which often fail due to patients growing resistance to therapy over time. In a previous from TMEM165 has been shown to be a breast cancer specific protein and has been linked to congenital disorders of glycosylation making it a possible biomarker for breast cancer. In this study, we inhibit estrogen-receptors in estrogen-receptor-positive breast cancer cells and analyze TMEM165 gene expression. Our hypothesis is that TMEM165 gene expression increases in ER-negative breast cancer cell lines.

37B-U. Genetic Causes of Craniosynostosis. Jasmine <u>Mckissick</u> and Yuri Zarate. *Pediatrics, UAMS, Little Rock, AR* 72205.

Craniosynostosis, the premature fusion of bones in the skull, can cause craniofacial abnormalities, abnormal growth of and pressure on the brain, as well as secondary developmental and behavioral issues. Craniosynostosis can be a diagnosis on its own or diagnosed as a part of a syndrome and can involve single or multiple sutures. Genetic testing can be used to confirm a diagnosis, help physicians discriminate among similar syndromes, and guide recommendations for the best treatment plan. Genetic counselors can also use genetic testing to help educate patients and their families about current and future health conditions and health decisions. The objectives of this study were to characterize craniosynostosis patients at a pediatric hospital in the south, assess the amount of genetic testing done on these patients and their results, and increase our knowledge of the varying diagnoses of syndromic craniosynostosis. As a retrospective analysis study, we characterized 143 craniosynostosis patients (67% males) that underwent craniofacial reconstructive procedures (97%) or were recommended to have reconstructive procedures (3%). I collected patient information from the hospital's medical record database and constructed a spreadsheet which categorized demographics, surgery information, genetic testing performed, health conditions, and family history. Fortyone patients (29%) had multiple sutures affected with the sagittal suture being the most common (33%). Most craniofacial reconstructive procedures (80%) were performed during infancy (median age of six months) with multiple procedures needed in almost 30% of cases. Testing for abnormalities of the FGFR1, FGFR2, FGFR3, and TWIST genes alone or in combination with other genes related to craniofacial development was the most common genetic test performed (30 patients, 56% of those tested), followed by microarray studies (28 patients, 52% of those tested). A final diagnosis was achieved in 29 patients (20%), with 15 having well described craniofacial syndromes (Crouzon, Saethre-Chotzen, Pfeiffer, Apert, and Carpenter). Not surprisingly, patients with multiple affected sutures were more likely to have been diagnosed with a genetic syndrome (49%) compared to those that had a single suture affected (9%) and patients with developmental delay or other birth defects were more likely to have genetic testing done. In summary, a genetic diagnosis was reached in 20% of patients who had or were recommended for craniosynostosis repair in this study. Considering that only 38% of patients underwent genetic testing, the high yield of abnormal results (29/54=54%) suggests that genetic evaluation could be

particularly important in this group of patients. Also, in addition to several less commonly diagnosed syndromes associated with craniosynostosis, we found other conditions that have not been previously linked to this problem. Other conclusions from this study would be that genetic testing is a valuable resource for clinical diagnoses of craniosynostosis and that being implemented more frequently when seeing abnormal facies, developmental delays, and/or other health conditions may shed more light on the varying phenotypes of craniosynostosis syndromes.

38A. GSAR: Bioconductor package for gene set analysis in R. <u>Yasir Rahmatallah</u> and Galina Glazko. *Biomedical Informatics. UAMS, Little Rock, AR* 72205.

Gene set analysis (in a form of functionally related genes or pathways) has become the method of choice for analyzing omics data in general and gene expression data in particular. There is a multitude of tests available, ranging from aggregation tests that summarize genelevel statistics for a gene set to true multivariate tests, accounting for intergene correlations. Most of them detect complex departures from the null hypothesis but when the null hypothesis is rejected the specific alternative leading to the rejection is not easily identifiable. GSAR is an open-source R/Bioconductor software package for gene set analysis (GSA). It implements multivariate nonparametric statistical methods testing a complex null hypothesis against specific alternatives, such as differences in mean (shift), variance (scale), or net correlation structure. Multivariate generalizations of the Wald-Wolfowitz and Kolmogorov-Smirnov statistical tests are implemented. The package also provides a graphical visualization tool, based on the minimum spanning trees, for correlation networks to examine the change in the correlation structures of a gene set between two conditions and highlight influential genes (hubs).

38B-U. Does exposure to different concentrations of caffeine affect Dictyostelium development? Sandhya Baviskar, <u>Loi Bui</u>, and Allyson Frantzen. *Developmental Biology, UA Fort Smith, Fort Smith, AR* 72904.

The soil amoeba, Dictyostelium discoideum, has been one of the most popular model organisms in molecular biology. Due to its simple life cycle, small genome size, and availability, it is used to conduct experiments in cell and molecular biology and developmental biology. Caffeine is the world's most widely used psychoactive drug that stimulates central nervous system. It can alter the physiology, mood, and behaviors of our body. The goal of this project is to observe how caffeine affects Dictyostelium development. Dictyostelium cells would be allowed to undergo development by placing them on starvation plates with different caffeine concentrations. Dictyostelium development would be observed at different time points during development and compared with the control starvation plates Based on preliminary data, we hypothesize that higher concentrations of caffeine would inhibit Dictyostelium development.

39A-U. Evolutionary conservation of axon guidance: midline repulsive signaling by Robo family receptors in mice and flies. <u>Alli Loy</u> and Tim Evans. *Biological Sciences, University of Arkansas, Fayetteville, AR* 72701.

As the nervous system develops in animal embryos, neuronal axons are guided to their synaptic targets by extracellular cues that signal through axon guidance receptors expressed on the surface of the axon. In animals with bilateral symmetry, one of the most important decisions made by nearly every axon in the embryonic nervous system is whether to stay on its own side of the body, or to cross the midline and connect to cells on the opposite side. The Roundabout (Robo) family is an evolutionarily conserved group of axon guidance receptors that regulate midline crossing in a wide range of animal groups, by signaling midline repulsion in response to their ligand Slit. Despite their strong evolutionary conservation, it is unknown if the mechanisms of Robo signaling are conserved across different species. Can Robo receptors from mice regulate axon guidance decisions in Drosophila embryos, or do species-specific differences exist in the cellular signaling mechanisms by which Slit and Robos regulate midline crossing? To investigate the evolutionary conservation of Robo signaling mechanisms, we are using the GAL4/UAS system in Drosophila to express Robo receptors from mice in fly neurons during embryonic development. We find that mammalian Robo receptors can repel axons from the midline in Drosophila embryos, which suggests that the mechanisms by which they signal midline repulsion are conserved in insects and mammals.

39B. A Zinc Finger Nuclease Based Strategy for an efficient excision of selection marker gene from rice transgenic plants. <u>Bhuvan Pathak</u> and Vibha Srivastava. *CSES, University of Arkansas, Fayetteville, AR* 72701.

Due to a global surge in the food production, developing crop varieties with multiple traits like disease resistance, improved agronomic quality and nutritional content is highly required. These traits can be rapidly introduced by transgenic/cisgenic/intragenic transformation approaches. These approaches rely on the use of selection marker genes to isolate the genetically modified (GM) cells from a population of non- modified cells through tissue culture. After the selection of the GM cells, these selection marker genes are not desired in their end products (GM plants). Also, the presence of marker genes in the field grown GM crops is highly undesirable. Here, we present a Zinc Finger Nuclease (ZFN) based strategy for the excision of the selection marker genes from the rice model. We have successfully tested that ZFN could induce a double stranded break in the rice genome with 13% efficiency. The ZFN lines expressed under heat inducible promoter (HSP: ZFN) were generated. The expression analysis (RT-qPCR) showed 64-14000 fold increase in the ZFN expression under heat inducible condition compared to their non- heat induced controls. The target lines containing the marker genes flanked by ZFN target sites (CCR5 target lines) have also been generated. The CCR5 target lines and HSP: ZFN lines are currently being crossed to evaluate the efficiency of ZFN in excising the marker genes.

40A. A Comprehensive Assessment of Salmonella Typhimurium Genes Involved in Response to Hydrogen Peroxide. <u>Sardar Abdullah</u> and Young Min Kwon. *Cell* and Molecular Biology, University of Arkansas, Fayetteville, AR 72701.

Salmonella is a Gram-negative bacterium that infects a wide range of hosts. The non-typhoidal Salmonella Typhimurium causes enteritis. The bacteria can survive and replicate in macrophages. An essential mechanism uses by the macrophages to kill and eradicate Salmonella is production of reactive oxygen species (ROS). In vitro Salmonella growth in the presence of hydrogen peroxide (H2O2) would be a reasonable model to understand the molecular mechanism of Salmonella survival inside the macrophages. Although the product of some genes that have a role in reducing the toxicity of H2O2 are known in the Salmonella, the global genes behind the adaptation and survival of the bacterium under H2O2 is remained elusive. In this work, we used Tn-seg method to determine the candidate genes that have a role in response to H2O2 of the Salmonella. A highly saturated transposon insertion library was grown in vitro in three growth conditions; Luria-Bertani broth (LB) medium, and the LB contains either 2.5 or 3.5 mM H2O2. We identified a comprehensive list of putative genes that make bacteria tolerant to the ROS. The consensus identified genes in response to both H2O2 conditions were 137 genes. The top 19 genes were hscA, rbsR, fepD, efp, oxyR, polA, ybaD, aroD, ruvA, xthA, dps, aroB, uvrD, tonB, uvrA, aroK, ybbM, lon, and proC. The top enriched pathways were nucleotide repair and degradation, purine and pyrimidine metabolism, and aromatic amino acid biosynthesis. The identified genes by the Tn-seq were verified by using single mutant assays. Of the 137 identified genes, 49 individual mutants were assayed and 41 were showed to have a role in response to the H2O2. The data were indicated that as the concentration of H2O2 elevates, the fitness of the required genes to the H2O2 reduce. This list of genes could have a role in making H2O2 less toxic and allow the Salmonella to survive and replicate in presence of

mM H2O2 in vitro. The identified candidate genes can be exploited to develop new antimicrobial drugs and deepen our understanding about survival of the bacteria in the macrophages.

40B-U. Hind Limb Suspension and Antigravity. <u>Kristen</u> Jones, Brent Hill, Charles Dekard, and Azida Walker. *Biophysics, University of Central Arkansas, Conway, AR* 72035.

Simulated microgravity is often proposed to correlate with a decreased bone density and strength. This study was designed to simulate spaceflight through hind limb suspension system in mice. We subjected 2 month old mice to OVX and SHAM surgeries and evaluated the overall effects of the surgeries and the hind limb suspension on the bones using a three-point bending method, bone dimensions and evaluating their food and water intake. Body weight and food and water intake were monitored throughout the research. In previous research, we found that the SHAM mice bones could withstand a significantly greater amount of pressure before breaking versus the OVX mice bones. We expect to see the same results as we break the OVX and SHAM mice bones that were involved in the HLU experiment. We are surprised to see that the body weight was unhanged from the time that the mice were suspended to the time that they were sacrificed. Our study demonstrates what effects antigravity and OVX has on physical parameters of the mice's bones as we assess the strength of the bones.

41A-U. Cadherin 18 Localization and Interacting Partners. <u>Scotty McKay</u> and Calin Marian. *Biology Department, University of Central Arkansas, Conway, AR* 72035.

Cadherins are calcium dependent cell adhesion proteins that are generally located on the cell membrane. Type I cadherins, which are much more well-known than Type II, play a large role in cell-cell adhesion. Type II cadherins lack the HAV coding region present in Type I cadherins which plays a critical role in the cell's adhesion functions. Prior research has suggested that some Type II cadherins may play major roles in cancer and early morphogenesis. By learning more about the roles that Type II cadherins play in living cells, we could gain a greater understanding of bodily processes and disease development. The protein that we are specifically interested in is a Type II cadherin known as cadherin 18 (CDH18). We will begin this project by looking at the cellular distribution of cadherin 18 in human embryonic kidney cells that were engineered to over-express this protein as well as a GFP tag. We will then examine how these proteins interact with other proteins using techniques such as immunocytochemistry, immunoprecipitation, and mass spectroscopy.

41B-U. Steroid Signaling Mediates Longevity Responses to Dietary Restriction in C. elegans. <u>Ashley</u> <u>Henderson</u>, Kaitlynn Butler, and Mindy Farris. *Biology Department, University of Central Arkansas, Conway, AR* 72035.

Caenorhabditis elegans is an excellent model for longevity experimentation and is predictably shown to have an extended lifespan under dietary restriction (DR) conditions. In addition to assessments of lifespan, through applying varying degrees of stressors to the worms, their stress response as a function of age can be measured. We studied heat stress and dietary restriction applied to young (1-day old) wild type (N2) worms and worms with a mutation in an isoform of 3βhydroxysteroid dehydrogenase, hsd-3. It has been previously observed that worms exposed to a heat stressor exhibit increased thermotolerance under dietary restriction (DR) conditions, using bacterial deprivation (BD), than with normal growth media (NGM). BD conditions can be technically difficult to use experimentally, as many worms are lost to non-agerelated deaths. We investigated BD using an alternative method: solid minimal media (MM) containing only agar and NaCl. We compared lifespans and heat stress resistance for N2 and hsd-3 worms using BD, NGM, and MM, with and without OP50 E. coli. Parent populations of both strains were kept nonstarved at 20°C. L4 animals were selected on day 0, and were kept at 20°C throughout their lifespan. Adults were moved away from progeny and the number alive was tallied until all worms had died. For the heat stress assay, the worms were put at 35°C for seven hours on day 1, then moved back to 20°C for the remainder of the assay. During the initial lifespan trials conducted, the N2 worms had shorter average lifespans than the hsd-3 mutants on the BD plates, although this result is not statistically significant. Surprisingly, the fed hsd-3 worms lived longer than the hsd-3 worms under DR, suggesting that hsd-3 might be required for DR-mediated lifespan extension. During the heat stress assay, the hsd-3 mutants still outlived the N2 strain, however the worms on the BD media had, on average, the longer lifespan. In addition to showing the effects of hsd-3 signaling in DR pathways, we show that the MM condition is comparable to BD, and easier to use in the laboratory.

42A-U. Parkinson's Disease: A Mitochondrial-linked Etiology. Stephanie Dayer, Ethan Chernivec, <u>Avery</u> Rasberry, and Kari Naylor. *Biology Department, University of Central Arkanss, Conway, AR* 72035.

Parkinson's disease is a neurological degenerative disorder that is characterized by the death of dopaminergic cells in the zona compact of the substantia nigra. The etiology of Parkinson's disease remains relatively unknown with much of the recent research indicating a relationship to mitochondrial function due to the characteristic selective loss of complex I activity, as well as the increase in ROS production (Keeney, et al. 2006). Various mutations have been linked to the development of Parkinson's disease in genes such as PARK, PINK-1, and LRRK2, among others that code for mitochondrial associated proteins (Rasheed, Tabassum and Parvez 2015). Certain insecticides and fungicides have been experimentally shown to generate specific characteristics of Parkinson's disease in vivo and in vitro, such as MPTP and rotenone. Establishing model organisms for Parkinson's research is essential for discerning etiology and pathogenesis. Due to rotenone's establishment as an inducer of Parkinsonism it was selected as our drug of choice to evaluate Dictyostelium discoideum's functionality as a model organism for idiopathic Parkinson's disease research. In order to evaluate Dictyostelium as a model organism for Parkinson's disease we must confirm the presence of characteristics noted in Parkinson's disease, such as complex 1 inhibition, high ROS production, mitochondrial dysfunction and microtubule assembly interference. Thus far we have examined cell viability for multiple strains of Dictyostelium discoideum and determined their LC50s. Preliminary data indicates that rotenone inhibits fusion in exposed cells, as well as reduces mitochondrial velocity, suggesting a defect in microtubule organization.

42B-U. Steroid Signaling Mediates Longevity Responses to Dietary Restriction in C. elegans. <u>Ashley</u> <u>Henderson, Kaitlynn Butler</u>, and Mindy Farris. *Biology Department, University of Central Arkansas, Conway, AR* 72035.

Caenorhabditis elegans is an excellent model for longevity experimentation and is predictably shown to have an extended lifespan under dietary restriction (DR) conditions. In addition to assessments of lifespan, through applying varying degrees of stressors to the worms, their stress response as a function of age can be measured. We studied heat stress and dietary restriction applied to young (1 day old) wild type (N2) worms and worms with a mutation in an isoform of 3βhydroxysteroid dehydrogenase, hsd-3. It has been previously observed that worms exposed to a heat stressor exhibit increased thermotolerance under dietary restriction (DR) conditions, using bacterial deprivation (BD), than with normal growth media (NGM). BD conditions can be technically difficult to use experimentally, as many worms are lost to non-agerelated deaths. We investigated BD using an alternative method: solid minimal media (MM) containing only agar and NaCl. We compared lifespans and heat stress resistance for N2 and hsd-3 worms using BD, NGM, and MM, with and without OP50 E. coli. Parent populations of both strains were kept nonstarved at 20°C. L4 animals were selected on day 0, and were kept at 20°C throughout their lifespan. Adults were moved away

from progeny and the number alive was tallied until all worms had died. For the heat stress assay, the worms were put at 35°C for seven hours on day 1, then moved back to 20°C for the remainder of the assay. During the initial lifespan trials conducted, the N2 worms had shorter average lifespans than the hsd-3 mutants on the BD plates, although this result is not statistically significant. Surprisingly, the fed hsd-3 worms lived longer than the hsd-3 worms under DR, suggesting that hsd-3 might be required for DR-mediated lifespan extension. During the heat stress assay, the hsd-3 mutants still outlived the N2 strain, however the worms on the BD media had, on average, the longer lifespan. In addition to showing the effects of hsd-3 signaling in DR pathways, we show that the MM condition is comparable to BD, and easier to use in the laboratory.

43A. Impact of nutrient availability on protein misfolding in C. elegans. <u>Landon Gatrell</u> and Mindy Farris. Department of Biology, University of Central Arkansas, Conway, AR 72035.

Alterations in protein folding, due to mutations and/or normal cell senescence, may lead to aggregation of misfolded proteins, ultimately leading to toxicity and cell death. Protein aggregation has been shown as a normal consequence of aging, but it is largely associated with age-related disease, particularly neurodegenerative diseases like Alzheimer Disease (AD) and Huntington Disease (HD). The model organism Caenorhabditis elegans has been extensively used to study aging and progression of these neurodegenerative diseases. Under normal circumstances, glucose enrichment shortens C. elegans lifespan; however, recent research suggests that glucose actually provides some protection against cell stress, including proteotoxicity related to aggregation. Using C. elegans, we will investigate glucose-mediated neuroprotection against protein misfolding phenotypes including accumulation of ubiquitin-tagged protein aggregates and cell death.

43B. Regulation of symbiotic gene expression in rice. Jackie Thomas, H Ram Kim, Ryan Hiltenbrand, Hannah McCarthy, Alex Howell, Raj Singh, David Simulinda, Arijit Mukherjee. *Biology Department, University of Central Arkansas, Conway, AR* 72035.

Major advances in the Human Microbiome Project have shown the significance of the microbial community in our gut. Interestingly, the microbial community in the ground is as important as the one in our guts. Soil microbes especially fungi and bacteria cycle nutrients and water to plants, to our crops, the source of our food, and ultimately our health. Unfortunately, the soil microbiota is under constant threat due to overuse of fertilizers, fungicides, pesticides, and heavy tillage to boost crop productivity. Nutrient pollution (too much nitrogen and phosphorus) in water is one of America's most widespread, costly and challenging environmental problems, which can have diverse and far-reaching impacts on public health, the environment, and the economy (U.S. Environmental Protection Agency). For instance, excess nitrogen from fertilizer run-offs in drinking water can cause serious health problems like rashes, stomach or liver illness, respiratory problems, neurological affects, reproductive and developmental risks, and even cancer (National Institutes of Health). Clearly we need alternatives to these harmful fertilizers for improving crop productivity. Biological Nitrogen Fixation (BNF) is increasingly being viewed as a viable alternative for supplying N to plants and improving yield and overall plant health. Several reports have shown that in rice the BNF comes from species of Azospirillum, Herbaspirillum, and Azorhizobium etc. The replacement of fertilizers with N-fixing plant growth-promoting bacteria could save billions of dollars per harvest. Therefore, the use and improvement of such a promising agricultural tool could provide enormous health, economic, and environmental benefits. Unfortunately, our understanding of how plants respond to rhizospheric endophytic bacteria is very poor. We clearly need specific studies that will identify host plant genes during interactions with rhizospheric bacteria that can fix N for the plant. Our specific objective for this project is to identify differential gene expression in rice roots during colonization by N fixing bacteria, Azorhizobium, Azospirillum and Herbaspirillum. This will identify candidate plant genes involved during symbioses with these beneficial bacteria. Towards these goals, we have already set up an experimental system to study these host-microbe interactions. Recently, we performed an RNA Sequencing (HiSeq2500 PE 2x100 bp) experiment in rice roots upon colonization with Azorhizobium caulinodans ORS571. We identified 1135 differentially expressed genes and we validated the expression pattern of a few genes via RT-PCR. In the future, we aim to identify genes in the host plant that regulate this interaction and characterize the genetic pathway. We have also initiated similar studies between rice-Azospirillum brasilense and rice-Herbaspirillum seropedicae. In the long term, these studies will help us better understand how the host plant recruits its genes during interactions with these beneficial bacteria and improve its own health and contribute to our health.

44A-U. FtsZ Homolog, FszB's Role in Dictyostelium Discoideum Mitochondrial Dynamics. Kari Naylor. <u>Ericka Vogel & Pristine Pittman</u>. *Cell Biology, University of Central Arkansas, Conway, AR* 72035.

It is believed that mitochondria were once independent entities, but later were ingested by a cell and eventually became an essential part of that cell—for it provided a major source of ATP. As more knowledge was acquired regarding mitochondria, scientists learned that malfunctions in mitochondrial dynamics (fission and fusion) contribute to many diseases. In particular, diseases that affect the nervous system like Parkinson's and Alzheimer's. In order to advance this research, it is important to begin with the foundation. While human mitochondria no longer utilize the mitochondrial division associated protein filaments like FtsZ, these filaments do occur in protists—an organism, in regards to cladistics, that is closer to the ancient cell that could have ingested what eventually became the mitochondria. In our model organism, Dictyostelium discoideum, there are two FtsZ homologs, FszA and FszB. These appear to play a role in mitochondrial division in these cells. We have determined the rates of fission and fusion to be significantly lower in cells overexpressing GFP-FszB. Interestingly GFP-FszB appears to localize to almost all identified fission and fusion events. We are currently determining the rate of mitochondrial motility when GFP-FszB is overexpressed. With these preliminary results we suggest that this protein filament inhibits mitochondrial dynamics. This work allows us to better understand the mechanisms that could potentially disrupt or regulate mitochondrial disease.

44B. Investigating the role of the dynamin-like proteins (Dlps) in the mitochondrial dynamics of Dictyostelium discoideum via cytoskeletal disruption. <u>Nicholas West</u> and Kari Naylor. *Biology Department, University of Central Arkansas, Conway, AR* 72035.

Mitochondria are dynamic organelles, hypothesized to be derived from an ancestral symbiosis between freeliving prokaryotes, which eventually gave rise to eukaryotic cells. These organelles perform vital metabolic functions such as oxidative phosphorylation to form ATP for cellular energy; programmed-cell death for cell maintenance, development, and differentiation; and the regulation of calcium ion storage for cellular pathways. Their tubular structure and, thus, their functional capabilities are maintained through the dynamic processes of fission and fusion. Proteins embedded in the inner and outer mitochondrial membranes are primarily responsible for these events. Adapter proteins, proteins related to the dynamin superfamily (DRPs), and the actin and microtubule cytoskeleton are associated with the regulation of mitochondrial morphology. Disruption of mitochondrial morphology is strongly related to dysfunction of the organelle itself, which has been strongly linked to various neurodegenerative diseases, cardiovascular diseases, and complications related to diabetes. In our research, we are investigating the role that the dynamin-like proteins (Dlps) play in regulating mitochondrial morphology, fission, fusion, and motility through the disruption of the actin and microtubule cytoskeleton. We collected a minimum of 50 cells from

the wild-type AX4 and the mutant dlpA-, dlpB-, and dlpC- strains of Dictyostelium discoideum, in order to quantify the morphology of the mitochondria and the cytoskeleton when treated with the drugs Latrunculin B or Nocodazole which are designed to depolymerize the actin and microtubule cytoskeleton, respectively. We also examined fission and fusion events as well as mitochondrial velocity and percent moving for treated and untreated cells between the wildtype and knockouts. Our preliminary results indicate that DIpA plays a role in regulating the actin cytoskeleton, which is complementary to the literature, while fission and fusion are upregulated. This work will provide additional characterization of the dynamin-like proteins and the relationship they have with the mitochondria and cytoskeleton.

45A-U. Modeling the Atomistic Structure and Dynamics of the Chloroplast Signal Recognition Particle. <u>Mitchell Benton</u> and Mahmoud Moradi. *Chemistry Department, University of Arkansas, Fayetteville, AR* 72701.

We have characterized the structural dynamics of the chloroplast signal recognition particle and its stability using atomistic biomolecular simulations. The chloroplast signal recognition pathway provides a method whereby light-harvesting proteins (LHCPs) can be inserted into the thylakoid membrane. In a photosynthetic organism, most proteins are synthesized outside of the thylakoids. Consequently, these light harvesting proteins must possess a "flag", usually an Nterminal amino acid sequence, which can help aid targeting to the thylakoids. The particular proteins that can recognize these amino acid signal sequence are called signal recognition proteins, or SRPs. One of the particular SRPs associated with targeting in the chloroplast is the cpSRP43. Additionally, cpSRP54 is a GTPase that has the capacity to increase the targeting efficiency of cpSRP43 when bound to the cpSRP43 peptide. To characterize their conformational dynamics at the atomic level, we used modeling and molecular dynamics simulations of both the isolated cpSRP43 and the cpSRP43/cpSRP54 complex. These computational models allow us to obtain a highly detailed perspective on the conformational landscape of the proteins. The models are generated using multiple techniques of molecular modeling, docking, and all-atom molecular dynamics. The models are dynamic, so we can observe how a protein changes its conformation over time. In addition, we were able to induce certain hypothetical transitions by pulling particular domains to observe how the conformation changes over time. We use a collective variable based algorithm to apply forces on particular protein domains, and we use time-dependent harmonic restraining to move the domains towards or away from each other. We can manipulate how long it takes to move those domains towards each other, and

how the strength of the force by which the domains are pushed or pulled. These computational experiments can be used to test different hypotheses in a comparative manner. The information gained from this project is not only important in gaining a unique knowledge of photosynthetic pathways, but can also be applied to a number of analogous biological systems.

45B-U. Dissecting the Molecular Mechanism of Action of a Novel Antifungal Peptide. <u>Cody Bullock</u>, David S. McNabb, and Ines Pinto. *Biological Sciences, University* of Arkansas, Fayetteville, AR 72701.

Candida species represent the predominant cause of fungal infections in humans, ranking as the fourth most common hospital-acquired infection. New antifungal therapies are needed as current treatments of Candida infections are not effective against all species. Moreover, the mortality rate from systemic Candida infections ranges from 35-40%. Antimicrobial peptides are known to kill both bacterial and fungal pathogens. Humans produce a number of peptides as part of their innate immune response. The Histatins are a family of naturally-occurring peptides secreted into the oral cavity and display significant antimicrobial activity. Histatin 5 is a twenty-four amino acid peptide that displays strong antifungal activity. Studies from our laboratory have identified small histatin-derived peptide, KM29, which yield fungicidal activity 10-fold greater than Histatin 5 against a number of Candida species. To understand the molecular mechanisms by which these peptides kill yeast, we are using Saccharomyces cerevisiae as a genetically tractable model to identify mutations that confer increased resistance or sensitivity to the peptides. We have developed a system to carry out a whole genome screen for increased sensitivity or resistance to KM29. We will present preliminary data on several gene clusters identified, including mitochondrial function, plasma membrane/cell wall biogenesis, and various transporters.

Chemistry and Biochemistry

Friday Oral Platform Session

ORAL – 3:20. Utilizing a Mutated Taxus Benzoyltransferase (mTBT) as a Biocatalyst. <u>William</u> <u>Staton</u> and Irosha N. Nawarathne. *Math and Science* Department, Lyon College, Batesville, AR 72503.

The antineoplastic agents paclitaxel (Taxol[®]) and docetaxel (Taxotere[®]) are currently supplied commercially by plant cell fermentations which rely on a biological source. While the plant cell fermentations may be a viable source for Taxol, a more biotechnological method would be more effective to make Taxol analogues. Structure-activity-relationship studies have led to the development of highly promising paclitaxel analogues compared to the parent molecule through acyl group modifications. Taxol pharmacophore includes all the acyl groups around the tricyclic core. Therefore, the acyl group modifications at C-10, C-2, C-4, and C-13 hydroxy-, and C-3' amino- positions are targets for developing efficacious paclitaxel analogues. The enzyme mTBT, has been observed to be able to catalytically produce several 7,13-0,0-diacetyl-2-0-acyl-2-O-debenzoylbaccatin III analogues. This shows the broad specificity of mTBT, suggesting that a plethora of 2-O-acyl variants of the antimitotic paclitaxel can be assembled through bio-catalytic sequences. The production of paclitaxel and related compounds can therefore be improved by understanding the biosynthesis of these metabolites in detail. We intend to probe into the effect of modifications on the C-7 group of the substrate on the productivity of mTBT. It has already been shown that an O-acetyl group on the C-7 is more productive over the substrate that has C-7 hydroxylated. This could imply that either the O-acetyl group may play a role in mTBT reaction or that the hydroxy group may hinder the same reaction. The fact that the C-7 seems to need a moiety that is not free hydroxyl group implies that the mTBT step occurs prior to the catalytic hydroxylation at C-7 in the biosynthetic pathway. By replacing the C-7 hydroxy group with hydrogen and utilizing the resulting C-7 deoxygenated analogue as a mTBT substrate, more information could be discovered about the timing of the 2-Obenzoyltransferase reaction in Taxol biosynthesis and its' importance in the biocatalytic production of Taxol analogues.

ORAL – 3:35. The Effect of Glutamine and y-Glutamylglutamine on NIH-3T3 Cell Metabolism. Nicholas S. Kowalkowski, Rosalind B. Penney, and Gunnar Boysen. Department of Chemistry, Ouachita Baptist University, Arkadelphia, AR 71998.

Although extensive research is being done on the subject, cancer metabolism is one field of study that can be considered still in its infancy. Understanding the metabolism of cancerous cells is critical for improving treatments and diagnostic tools. One metabolomic pathway of interest is the y-glutamyl cycle, which cells use to create y-glutamyl-amino-acids from glutathione and amino acids using γ -glutamyltransferase. This cycle allows for the easy transport of y-glutamyl-amino-acids through the cell membrane, where the cell can utilize the amino acid. A common amino acid is glutamine, which may be responsible for transforming NIH-3T3 embryonic fibroblast cells into cancer. For this experiment, it was hypothesized that the addition of glutamine will induce transformations in the NIH-3T3 cell line, and that the addition of γ -glutamylglutamine

would increase the number of transformations. For the first goal of the project, NIH-3T3 cells were left untreated or treated with 5mM L-glutamine and allowed to grow for 21 days. Transformations were seen on day ten of the experiment in glutamine-treated cells, but not in cells without glutamine. A "pretransformation" element was also identified and defined, and daily photographs taken over the course of a week demonstrated the visual process of transformation. The data confirm the importance of glutamine in inducing transformations in NIH-3T3 cells. For the second goal of the project, cells were grown in DMEM media with either 1mM, 2.5mM, or 5mM yglutamylglutamine solution or a combination of 1mM, 2.5mM, or 5mM γ-glutamylglutamine with 5mM glutamine solution. Contrary to the hypothesis, a decrease in the number of transformations relative to the prior experiment was experienced with the increase in y-glutamylglutamine. Minimal differences were observed with the inclusion of glutamine with most occurring in the 5mM y-glutamylglutamine. While the data would imply that a higher concentration of yglutamylglutamine would inhibit cell transformations, further research is required to identify the physiological concentration of the compound and to determine the role of γ -glutamylglutamine in human cells.

ORAL – 3:50. Synthesis and Analysis of Superparamagnetic Bridged Lanthanide (III)

Complexes. <u>Tia'Asia James</u>, Brian S. Dolinar, and Kim R. Dunbar. *Chemistry Department, UA Pine Bluff, Pine Bluff, AR* 71601.

Single molecule magnets (SMMs) are a class of molecular compounds that manifest superparamagnetic behavior below a discrete blocking temperature. The development of research in the field of SMMs promises to engender essential advancements in diverse applications, such as data storage, molecular spintronic, and quantum computing. In this project, attempts to synthesize [Dy(hfac)3]2(bptz), [Dy(hfac)3]2(Me4bpym), and [Dy(hfac)3]2(bmtz) (hfac =

hexafluoroacetylacetonate, bptz = 3,6-bis(2-pyridyl)-1,2,4,5-tetrazine, bmtz = 3,6-bis(2-pyrimidyl)-1,2,4,5tetrazine, Me4bpym = 4,4',6,6'-tetramethyl-2,2'bipyrimidine) are described. Synthesis of the neutral and radical form of these compounds will facilitate an understanding of the effects the radicals will have on the strength of the large spin-orbit coupling properties of dysprosium. Once both are synthesized, the neutral compound will be used as a comparison to the radical compound to compare their magnetic responses directly. [Dy(hfac)3]2(bptz) compound was structurally characterized by X-ray crystallography and its SMM properties were magnetically characterized by the SQUID magnetometry.

ORAL – 4:05. Detection of Helix Fraying in Transmembrane Helices with Interfacial Histidine

Residues. <u>Amanda Paz Herrera</u>, Fahmida Afrose, and Denise Greathouse. *University of the Ozarks, Clarksville, AR 72830; Chemistry Department, University of Arkansas, Fayetteville, AR 72701.*

Transmembrane helices of integral membrane proteins often are flanked by interfacial aromatic residues that may serve as anchors to aid the stabilization of a tilted transmembrane orientation. The synthetic neutral peptide GWALP23 (acetyl-

GGALW5LALALALALALALW19LAGA-ethanolamide) with two interfacial Trp residues has proved to be surprisingly well-behaved with minimal dynamic averaging in a stable transmembrane orientation in lipid-bilayer membranes of varying thickness. To further investigate the tilt, dynamics and pH dependence of GWALP23 with interfacial His residues, we have substituted G2 and G22 with histidines. In addition, to explore the fraying or uncoiling of the ends of the peptide, we have incorporated 2H-Ala labels at positions outside the core region of the peptide. By incorporating specific 2H-Ala labels at A3 and A21 we are able to compare the influence of interfacial residues on the extent of unwinding of the helix ends. Solid state 2H NMR spectra of macroscopically aligned bilayer samples will be prepared in DOPC lipid bilayers and in the presence of 10% and 20% cholesterol to observe how lipid-peptide interactions are affected when HWALP23 (acetyl-GH2ALW5LALALALALALALW19LAH22A-amide) interacts with the DOPC - cholesterol bilayers. The lipid bilayer integrity will also be assessed using 31P NMR spectra. To further understand the effects of histidine in transmembrane helices, we have also substituted W5 and W19 with histidine. GHALP23 (acetyl-GGALH5LALALALALALALH19LAGA-amide) also contains specific 2H-Ala labels at A3 and A21. "Geometric Analysis of Labeled Alanines" (GALA) will show the coiling or unwinding at the terminals for both HWALP23, and GHALP23. It is plausible that the helix fraying may be critical for the stability of the transmembrane helix orientation in the lipid bilayer membranes.

ORAL – 4:20. Conformational Protein Ensemble of the Calmodulin Ligand PEP-19. <u>Danica Ordonez</u>, Nick Rathke, Christian Mitchell, and Tori Dunlap. *Chemistry Department, University of Central Arkansas, Conway, AR 72035.*

Calmodulin (CaM) is a calcium sensing protein performing a regulatory function in an array of cell signaling pathways. CaM has a multitude of binding targets, some bind to its apo form, but CaM binds most targets while also bound to calcium ions. When bound to four calcium ions, calmodulin attains a conformational change that exposes hydrophobic residues, enabling CaM to induce α -helical structure in its intrinsically disordered ligands. Changes in these interactions have been associated with disorders such as Alzheimer's disease, Parkinson's disease, and cardiac hypertrophy. Calcineurin (CaN) is a CaM regulated serine/threonine phosphatase that has an α -helix induced binding region once bound to CaM. CaN also has a region C-terminal to its canonical CaM binding site that attains an α -helical structure upon CaM binding. We hypothesize that calmodulin has the ability to induce α -helical structure in regions outside its primary binding site in other CaM ligands such as PEP-19. PEP-19 is an intrinsically disordered, CaM binding, neuronal protein abundantly found in Purkinje cells of the cerebellum. When CaM is bound to PEP-19, the calcium binding kinetics of CaM are altered, changing the rate of calcium binding and release. A region in PEP-19 Nterminal to the CaM binding region has the potential to form an amphipathic α -helix much like the behavior exhibited by calcineurin bound to CaM. We used fluorimetry and FRET to study the conformational ensemble of PEP-19 and the ability of chaotropes and crowders to alter that conformational ensemble. We used the chaotropes urea and guanidine hydrochloride, the crowders PEG8000 and glucose, and the α -helix inducer trifluoroethanol (TFE) to compare the FRET of PEP-19 extended with the protein in a more globular or structure induced state.

ORAL – 4:35. DFT Study of the Selectivity of Phenylalanine Hydroxylase (PheOH). <u>Madison Perchik</u>, Larryn Peterson, and Mauricio Cafiero. *Chemistry* Department, Rhodes College, Memphis, TN 38112.

There are many molecules that act on dopamine and dopamine-like binding sites in enzymes and transport proteins. Some effects of these proteins are beneficial while others are detrimental. Our research group is designing inhibitors for this group of proteins. Phenylalanine hydroxylase (PheOH) is a tetradydrobiopterin-dependent monooxygenase that influences the rate determining step of converting phenylalanine into tryrosine by hydroxylating phenylalanine. Both phenylalanine and tyrosine are important components in the anabolism of dopamine. A deficiency of PheOH can cause hyperphenylalaninemia, which gives rise to phenylketonuria (PKU), a severe disease that can cause mental retardation if one's diet isn't strictly monitored. A suite of dopaminergic derivatives has been developed as potential inhibitors of the PheOH enzyme. The inhibitory effectiveness of these dopaminergic derivatives has been measured via in silico models in which the strength of interaction between each substrate and the enzymatic active site was analyzed. A crystal-structure of the PheOH active site, docked with thienylalanine, was isolated from the Protein Data Bank (PDB ID: 1KW0). The positions of novel dopaminergic derivatives were optimized in the active site using M062X/6-31G with implicit solvation

and with flexible amino acid side-chains. Interaction energies between the ligands and the protein were calculated using M062X and MP2 with the 6- 311+G* basis set. At present, none of the ligands examined bind as tightly as the natural substrate phenylalanine.

Chemistry/Biochemistry A – Saturday 8:00 – 9:00 Posters B – Saturday 9:15 – 10:15 Posters

(Posters designated "U" will be judged.)

101A-U. Expression and Purification of Calmodulin Binding Partner PEP-19. <u>Christian Mitchell</u> and Victoria Dunlap. Chemistry Department, University of Central Arkansas, Conway, AR 72035.

Calmodulin (CaM) is a calcium-sensing protein that plays a significant role in regulating enzyme activity. Often, CaM binds a disordered region and causes it to have an α -helical secondary structure. PEP-19 is a completely disordered 62 amino acid protein that is found in purkinje cells in the cerebellum. When PEP-19 binds to CaM it increases the rate at which calcium binds and releases altering calcium binding kinetics. To investigate PEP-19's conformational ensemble, we made and purified PEP-19 using E.coli and an expression method called autoinduction. Autoinduction is a unique method that uses a specific mixture and concentration of glycerol, glucose, and lactose, 5052, to cause the production of PEP-19 to occur without the need to monitor cell growth. Traditionally, autoinduction utilizes a specific autoinduction media which contains a complex variety of ingredients making it costly and troublesome to make. The original way we prepared PEP-19 was by using an IPTG method, which itself is inconvenient and time consuming due to the need to monitor cell growth. The IPTG method often requires the use of a simple, cost effective media called Terrific Broth (TB) that utilizes glycerol as the carbohydrate source. We hypothesized that we could utilize TB for autoinduction by replacing the standard glycerol with the 5052 mixture from autoinduction. Here we compare the expression of both CaM and PEP-19 utilizing the IPTG method, standard induction method, and autoinduction method using TB and 5052 to determine if utilization of TB and 5052 can provide a convenient, cost effective alternative to the IPTG and standard autoinduction methods.

101B-U. Effect of Calcium on the Native Conformation of PEP-19. <u>Nicholas Rathke</u> and Victoria Dunlap. *Chemistry Department, University of Central Arkansas, Conway, AR* 72035.

PEP-19 is a small, intrinsically disordered protein found primarily in the Purkinje cells of the cerebellum. PEP-

19's only known function is to regulate calcium binding to the protein calmodulin (CaM). PEP-19 accomplishes this by binding CaM, which in turn alters the kinetics involving calcium association and dissociation. PEP-19 has been observed to develop α -helix contingent upon CaM binding. CaM binds to over 300 known targets, with most of these interactions taking place when CaM is bound to calcium, making PEP-19's regulatory function critical to many processes. PEP-19 has been shown to guard against the effects of Alzheimer's disease, high intracellular calcium levels, and may even be implicated in the progression of Down's syndrome, due to it's locus being found on the 21st chromosome. Despite being intrinsically disordered PEP-19 has been shown to weakly bind calcium ions even in the absence of CaM, possibly contributing to its ability to protect against calcium fluctuations. We hypothesize that calcium binding to PEP-19 can alter PEP-19's native ensemble, possibly inducing structure. Thus we utilized fluorimetry to investigate possible differences in the conformational ensemble of PEP-19, in the presence and absence of calcium.

102A-U. Retinoic Acid Receptor Gamma Reciprocally Regulates Cellular Adhesion and Proliferation in K562 Cells. <u>Madison Lee</u>, Victoria Niedzwiedz, Rachel Mayo, and Melissa Kelley. *Chemistry Department, University of Central Arkansas, Conway, AR* 72035.

The interplay between cellular adhesion and proliferation is complex; however, integrins, particularly the $\alpha 5\beta 1$ subset, play a pivotal role in orchestrating critical cellular signals that culminate in cellular adhesion and growth. Retinoids modify the expression of a variety of adhesive/proliferative signaling proteins including, $\alpha 5\beta 1$ integrins; however, the role of specific retinoic acid receptors involved in these processes has not been elucidated. In this study, the effect of alltrans-retinoic acid receptor (RAR) agonists on K562 cellular adhesion, proliferation, and α 5 β 1 integrin cell surface expression was investigated. RARy agonist exposure increased K562 cellular adhesion to RGD containing extracellular matrix proteins fibronectin and FN-120 in a time- and concentration dependent manner, while RAR or RAR agonist treatment had no effect on cellular adhesion. Due to the novel RARydependent cellular adhesion response exhibited by K562 cells, we examined $\alpha 5$ and $\beta 1$ integrin subunit expression when K562 cells were exposed to retinoid agonists or vehicle for 24, 48, 72 or 96 hours. Our data demonstrates no significant differences in K562 cell surface expression of the α 5 integrin subunit when cells were exposed to RAR α , RAR β , or RAR γ agonists for all time points tested. In contrast, RARy agonist exposure resulted in a significant increase in cell surface $\beta 1$ integrin subunit expression within 48 hours that was sustained at 72 and 96 hours. Finally, we demonstrate that while exposure to RAR α or RAR β agonists have no

effect on K562 cellular proliferation, the RARy agonist significantly dampens K562 cellular proliferation levels in a time- and concentration- dependent manner. Our study is the first to report that treatment with a RARy specific agonist augments cellular adhesion to α 5 β 1 integrin substrates, increases cell surface levels of the β 1 integrin subunit, and dampens cellular proliferation in a time and concentration dependent manner in a human erythromyeblastoid leukemia cell line.

102B-U. Investigation of the Structural Stability of the Human Fibroblast Growth Factor using Hydrogen-Deuterium Exchange. <u>Elizabeth O'Daniel</u>, Julie Eberle, Suresh Kumar Thallapuranam. *Chemistry Department, University of Arkansas, Fayetteville, AR* 72701.

Human fibroblast growth factor 1 (FGF1) is an extracellular protein that plays a significant role in cell proliferation, angiogenesis, osteogenesis, and wound healing. Upon binding with the glycosaminoglycan heparin, the cofactor for which native FGF1 has a high affinity, the complex binds to its receptor on the cell membrane and initiates an intracellular signaling to induce the processes mentioned. Wild type FGF1 is known to be relatively unstable, in vitro, which makes it difficult to use in pharmacological applications. Previous research in the Kumar group revealed that a charge reversal (arginine to glutamic acid) mutation in the heparin binding pocket has marked effects on the protein's stability and bioactivity, as evidenced by increased stability and enhanced cell proliferation activity. In this study, using hydrogen-deuterium exchange kinetics, monitored by multidimensional nuclear magnetic resonance spectroscopy, we investigate the structural forces that contribute to the increased stability of this charged reversed FGF variant. The details of these findings will be presented.

103A-U. Effects of rolipram on the renal microcirculation during sepsis in the rat pup. <u>Alaa M.</u> <u>Shahare</u>, Clark R. Sims, Philip R. Mayeux. *Pharmacology and Toxicology, UAMS, Little Rock, AR* 72205.

Microcirculatory failure is a key event during sepsis that is believed to play a major role in multi-organ failure. Acute kidney injury is a complication of sepsis in infants that increases mortality. The phosphodiesterase (PDE)3 inhibitor milrinone is used in infant sepsis to improve cardiac function; however, its effectiveness in septic patients is limited. The goal of this study was to use the kidney as a model vascular bed to evaluate the effects of the PDE4 inhibitor rolipram on renal capillary perfusion and leakage. We developed a clinically relevant cecal ligation and puncture (CLP) sepsis model in rat pups 17-18 days old to model human infant sepsis. At 18h post sepsis (CLP) or sham surgery (Sham) pups were re-anesthetized with isoflurane. The left kidney was exteriorized and placed on the stage of an inverted microscope to visualize cortical capillaries. Five 10s videos from each animal were captured. Capillaries were analyzed for perfusion and categorized as having Continuous, Intermittent or No Flow. Capillaries with continuous flow were analyzed for red blood cell (RBC) velocity. Evans Blue Dye (EBD) (1% in saline; 2 mg/kg iv) was used to assess vascular leakage (1). To mimic the clinical setting where patients are treated only after the onset of symptoms, rolipram was administered at 6h post CLP. A decline in renal capillary perfusion occurred by 6h post sepsis. A dose-response study with rolipram (0.1-1.0mg/kg, ip, saline+0.5% DMSO) indicated 0.1mg/kg as the lowest most efficacious dose to improve perfusion at 6h. This dose was then tested with delayed administered at 6h post CLP. At 18h post CLP rolipram increased the percentage of capillaries with continuous flow (Sham, 72±4%; CLP, 46±5%; CLP+rolipram, 70±1%; n=5-6; P<0.05 compared to CLP) and improved RBC velocity (Sham, 217±5µm/sec; CLP, 119±10µm/sec; CLP+rolipram, 246±16µm/sec; n=5; P<0.05 compared to CLP). Rolipram also reduced capillary leakage (EBD uptake; Sham, 4.4±1.5ng/g; CLP, 12.6±2ng/g; CLP+rolipram, 6.9±2ng/g; n=5; P<0.05 compared to CLP). Sepsis in this infant model produces a rapid decrease in renal microvascular perfusion and RBC velocity. Sepsis also increases vascular permeability. Rolipram mitigated all of these microvascular defects even with delayed administration. These findings suggest that combination therapy with inhibitors of PDE4 and PDE3 may be more efficacious in the septic infant because PDE4 inhibitors also protect against overall microvascular perfusion and microvascular leakage. References 1. Holthoff JH, Wang Z, Patil NK, Gokden N, Mayeux PR (2013) J Pharmacol Exp Ther 347:357-364.

103B-U. Lectin affinity chromatography and Immunoextraction as a tool to study the effect of glycosylation on drug binding property of α 1-acid glycoprotein (AGP). <u>Kenan Dzide</u>, Chenhua Zhang, and David Hage. *Chemistry Department, UA Pine Bluff, Pine Bluff, AR 71601.*

There are nearly 3 million cases of Arrhythmia per year in the U.S. Cardiac Arrhythmia occurs when electrical impulses in the heart have an abnormal rhythm. In addition, 610,000 people die annually in the U.S. due to heart attacks. Specific pharmaceuticals such as disopyramide and warfarin are known to alleviate abnormal heart rhythms and heart attacks; respectively. Alpha1- acid Glycoprotein (AGP) is an acute phase glycoprotein of the human body that acts as an important carrier protein for many of these basic pharmaceuticals. AGP has heterogeneous glycosylations which consist of three different types of glycan structures: di-, tri-, and tetra- antennary branched complex-type glycans. It is our long term goal to analyze how these branchings can affect its drug binding properties. Lectin affinity chromatography and immunextraction will be used as a tool to study the effect of glycosylation on its drug binding properties. Concanavalin A lectin affinity chromatography will be used to separate AGP into glycoforms with different degrees of branching. These glycoforms will be collected and further captured into an anti-AGP immunoextraction microcolumn. Disopyramide will be used as a model drug to investigate the interaction of this drug with the captured AGP glycoforms.

104A-U. Ruthenium Complexes are pH- Activated Metallo Prodrugs Due to Photodissociation under Acidic Conditions. <u>Sydney A. Reed</u>, John A. Lundeen, Fengrui Qu, Elizabeth T. Papish, and Grant Wangila. *Chemistry Department, UA Pine Bluff, Pine Bluff, AR* 71601.

Ruthenium Complexes are pH- Activated Metallo Prodrugs Due to Photodissociation under Acidic Conditions Sydney A. Reed, John A. Lundeen, Fengrui Qu, Elizabeth T. Papish. University of Arkansas at Pine Bluff, University of Alabama. Abstract: Chemotherapy includes the use of toxic drugs that kill cancerous cells. Chemotherapy targets all rapidly dividing cells and kills malignant cells and also healthy ones as well. This leads to side effects such as nausea and hair loss. Cancer cells have a more acidic external pH than healthy cells. Most tumors are hypoxic and have decreased pH. Our goal is to form anticancer drugs that are activated by low pH and light to selectivity targets cancer cells. Three ruthenium compounds, [Ru(N,N)2(6,6'-dhbp)]Cl2 where (N,N) = bipyridine (bipy), phenanthroline (phen), and dioxinophenanthroline (dop), were synthesized and were investigated for activation at low pH and with light. For each compound, potentiometric titrations were done to determine the pKa values. The pKa values help determine at what pH value the compound will change form and be to active or inactive in aqueous solution. Also, studies were done to determine the rate of photodissocation at different pH values using UV-Vis spectroscopy. These compounds are also sent to collaborators for cell viability studies in cancer cell line culture. The combined data can indicate under what conditions our complexes will be activated.

104B-U. Measuring CO2 Emissions as a Basis for Understanding Indoor Air Quality and Room Ventilation. <u>Mercedes Winfrey</u> and Von P. Walden. *Chemistry Department, UA Pine Bluff, Pine Bluff, AR* 71601; Washington State University, Pullman, WA.

Washington State University (WSU) is collaborating to make Spokane, Washington a leader in smart city technologies. The Smart Cities Project will use smart sensor technology to provide better management of resources (such as energy and water) while also promoting health and well-being in the city. The Laboratory for Atmospheric Research at WSU is developing a sensor package for monitoring air quality for the Smart Cities Project, using various sensors to measure carbon dioxide, ozone, nitrogen dioxide, and particulate matter (particles from smoke and pollution). These sensors have been interfaced to a Raspberry Pi computer and are being mounted into a weather-proof 3-D printed container. As an initial test, we will measure the indoor air quality and ventilation rate with a costefficient CO2 sensor within a laboratory in the new PACCAR Environmental Technology Building at WSU. Carbon dioxide will be released into the lab periodically, and we will analyze the data on how the gas is disbursed within room. The rate at which the carbon dioxide dissipates in the lab will allow us to study the ventilation rate. The accuracy of the data from the sensor package will be compared to a more accurate and expensive LI-COR 820 Closed-Path CO2 sensors, which is currently being used in a national study of the indoor air quality of residential homes. Lastly, the various sensors will be mounted into the weather-proof container for eventual deployment on light posts in Spokane as part of the Smart Cities Project.

105A-U. Biased Agonism at CB2 Cannabinoid Receptors: Implications for Drug Development. <u>Rachel</u> <u>Hutchison</u>, Benjamin M. Ford, Lirit Franks, and Paul L. Prather. *Chemistry Department, UA Little Rock, Little Rock, AR 72204; UAMS, Little Rock, AR 72205.*

CB2 cannabinoid agonists are efficacious analgesics and show promise as anti-inflammatory and anti-cancer agents. CB2 receptors (CB2Rs) are G-protein coupled receptors (GPCRs) that produce effects via interaction with G-proteins and recruitment of b-arrestin. Studies have shown that b-arrestin may play a role in the anticancer activity produced by agonists acting via several GPCRs. Therefore, agonists that bias CB2R activation toward b-arrestin, relative to G-protein signaling, may exhibit enhanced cytotoxic effects in various types of cancer. Our laboratory recently reported a novel class of indole guinuclidine (IQD) compounds that bind cannabinoid receptors with relatively high affinity and act with varying intrinsic activity. The purpose of this study was to determine whether PNR-4-20, an agonist in this novel cannabinoid class, exhibits ligand bias at CB2 receptors. Biased CB2 signaling was determined by comparing the intrinsic activity of agonists to activate Gproteins and recruit b-arrestin in transfected CHO cells. Specifically, full concentration-effect curves for each compound in all assays were fit to the Black-Leff operational model of agonism to calculate transduction ratios (t/KA). Following bias determination, CB2 receptor down-regulation was then compared between cells chronically exposed to selected non-biased and biased agonists. PNR-4-20, a CB2 agonist from the novel IQD class, activated G-proteins less potently and efficaciously when compared to the established nonbiased CB2 agonist CP-55,940. In contrast, PNR4-20 recruited b-arrestin more potently, and with equal efficacy compared to CP-55,940. Indicative of enhanced CB2R coupling to b-arrestin, chronic treatment of cells with PNR-4-20 produced a more rapid down regulation of CB2Rs compared to CP-55,940. PNR-4-20 is a novel agonist that biases CB2R signaling toward recruitment of b-arrestin, relative to activation of G-proteins. Drugs developed by employing the PNR-4-20 scaffold may exhibit enhanced anti-cancer effects via selective interaction with b-arrestin, while minimizing potential adverse effects mediated by G-protein signaling.

105B-U. Copper(III) Amidomacrocyclic Catalyst Material as Platinum Alternative for Fuel Cell Applications. <u>Susan N. Boury</u>, Hunter A. Wayland, Anindya Ghosh. *Chemistry Department, UA Little Rock, Little Rock, AR 72204.*

Currently, platinum-based catalysts are the most efficient materials used for fuel cells at both electrodes. Platinum is costly due to its scarcity, and recent research has therefore been focused on investigating non-precious metal alternatives to replace platinum. A copper(III) amidomacrocyclic catalyst supported on graphene and coated with polydopamine was prepared and demonstrated potential for oxygen reduction reaction (ORR). Nanomaterial studies were performed to determine which carbon support best enhanced ORR activity, after which ratio studies were conducted to determine the optimum proportion of catalyst to graphene. Polydopamine, a bioinspired selfpolymerizing material, was then used to coat the nanocomposite of catalyst and graphene. The finished material may find application in commercialization of proton exchange membrane fuel cells (PEMFCs).

106A-U. Synthesis and photocatalytic activity of cellulose-based carbonaceous nanocomposites toward organic pollutants. <u>Dave Soni</u>, Bijay P. Chhetri, Charlette Parnell, and Anindya Ghosh. *Chemistry Department, UA Little Rock, Little Rock, AR* 72204.

Organic dyes are organic pollutants that are associated with environmental problems. Commonly used in the textile industries, 10-15 % of dyes are wasted in the dyeing process and released with effluent into the water. In order to remediate the water of these pollutants, various materials, such as cellulose, can be used in filtration devices. We used cellulose, an abundant and renewable polymer, as a carbon source to generate carbonaceous nanocomposites. The materials were produced through solid state mixing of starting compounds and pyrolysis in a tube furnace under inert nitrogen atmosphere. Following the same synthetic method, we also synthesized different nanocomposite materials by changing the ratio of cellulose and the nitrogen compounds. The doped materials were

characterized and analyzed through various methods including SEM, TEM, XPS, and BET. The photocatalytic activity of the materials was measured under visible light using various organic dyes. Control studies of the nanocomposites in dye in the absence and presence of light were also performed and the photocatalytic activity measured with an ultraviolet-visible spectrophotometer. We found high levels of dye removal in the experimental studies compared to the controls. Additional studies with different pH conditions and kinetics studies were also conducted. Our results indicated the N-doped cellulose nanocomposites are photocatalytically active towards organic dye removal from water. Therefore, integration of cellulose via a simple synthetic process proved to be sufficient for dye removal and could be further used for the pollution mitigation from wastewater.

106B-U. The Toxicity of Nanomaterials in Breast

Cancer Cells. <u>Kristen Gregory</u>, Vijayalakshmi Dantuluri, and Zeid Nima. *Center for Integrative Nanotechnology Sciences, UA Little Rock, Little Rock, AR* 72204.

Breast cancer is the second leading cause of cancer deaths in women and kills 40.000 women in the United States each year. Two important risk factors for developing breast cancer are age and family history. The stage of breast cancer determines the treatment a woman receives and can include: chemotherapy, radiation, and surgery. Chemotherapy and radiation have many side effects because they also kill noncancerous cells. Even with current treatments, there is always a chance that cancer cells will persist. I worked at the University of Arkansas at Little Rock in the Center for Integrative Nanotechnology Sciences. Our project was designed to test the effectiveness of the nanomaterials in killing the breast cancer cells. We cultured breast cancer cells (Cell line MCF7) for 24 hours with different concentrations of low-oxidized graphene, high oxidized graphene and gold nanorods. We measured cell growth at three, six, and 24 hours. For all three nanomaterials, cell proliferation decreased and as the concentration of nanomaterials increased. Based on these results, a high concentration of nanomaterials will likely decrease cell proliferation. The low-oxidized graphene treatment was most effective in killing breast cancer cells. Further work should include a longer time span, different concentrations and a different type of cancer cell lines.

107A-U. Developing FRET Assays to Study the Regulation of Fibroblast Growth Factor Binding to its Receptor. <u>Michael Crew</u>, Mamello Mohale, and Colin D. Heyes. *Chemistry Department, University of Arkansas, Fayetteville, AR* 72701.

The binding of Fibroblast growth factor (FGF) to its receptor (FGFR) is critical in angiogenesis, wound

healing, and signaling pathways. Unregulated FGF-FGFR signaling is known to cause different types of cancers such as bladder and breast, therefore understanding signaling regulation is vital. FGFs are heparin binding proteins which require an accessory molecule of Heparin/Heparin-sulfate (HS) which is important for the formation of the FGF-FGFR-Heparin complex. Signaling starts with the dimerization of two FGF-FGFR-Heparin complexes and the regulation of FGFR is thought to be by autoinhibition. Therefore, unregulated FGFR could lead to cancer. To the best of our knowledge, fluorescence resonance energy transfer (FRET) has not been utilized to study the interaction between FGF and its receptor FGFR. FRET works by labelling one protein with a donor dye and another protein with an acceptor dye. Maleimide dyes are commonly used for protein labelling because they can attach to the protein at specific sites through thiolether bond with cysteine residues. During FRET, the donor will transfer some if its energy to the acceptor which can be used to study the binding interaction, kinetics and other physical properties between FGF and its receptor. Preliminary results show that we were successful in performing cysteine site directed mutagenesis on FGF. Furthermore, FGF was effectively labeled with a series of maleimide dyes.

107B-U. Characterizing the Influence of a RAS Inhibitor on the Conformational Stability of Cdc42 and a Fast-Cycling Cdc42 Variant. <u>George Hristoskov</u> and Paul D. Adams. *Chemistry Department, University of Arkansas, Fayetteville, AR 72701.*

Cdc42Hs is a GTPase of the Ras superfamily, and it is responsible for regulation of the cell cycle. The Ras superfamily is a group of signaling proteins that are found on the cell membrane. Mutations of these proteins may cause cancer. Studying these proteins as well as their mutants will lead to a better understanding of how they may be influenced and inhibited. The purpose of this research project is to compare the conformation stability of the protein Cdc42Hs and its variant Cdc42Hs F28L, in the presence of an inhibitor molecule, ZCL278, which is known to interact with Cdc42Hs. Upon binding with GTP, Cdc42Hs becomes an active signaling molecule until the GTP becomes GDP through the GTPase cycle. Cdc42Hs F28L, a fast cycling variant of Cdc42Hs, undergoes this GTPase cycle at a faster rate which leads to cell transformation that may be negatively impactful to cell proliferation. The differences in unfolding in these proteins may yield a better understanding of the properties of these proteins. The affects that ZCL278 has on the conformational stability of Cdc42Hs and its mutant may lead to the discovery of a method regarding the inhibition of the harmful mutant while maintaining the conformation of Cdc42Hs.

108A-U. Regioselectivity and Activity of Ring-Opening Methathesis Polymerization Catalysts in Application to Homo-Coupling Olefin Metathesis. <u>Harper R. Grimsley</u> and Stefan M. Kilyanek. *Chemistry Department, University of Arkansas, Fayetteville, AR* 72701.

The activity and regioselectivity of the tungsten-oxo alkylidene W(O)(CHCMe2Ph)(DBMPO)2(MeCN) in homo-coupling is of interest to synthetic chemists looking for new olefin metathesis catalysts. Homocoupling represents dimerizing a substrate across its terminal olefins, liberating ethylene as a side product. One product that could be synthesized with the catalyst in question is a novel class of tethered complex which should be able to bind at two sites tetradentally. The spatial arrangement is of kinetic relevance, thus necessitating a Z-selective catalyst compatible with the substrate. This synthesis is actually of future interest to the Kilyanek lab at the University of Arkansas, as the product would be able to coordinate to two metal ions at once, creating a high local concentration of metal atoms even if the overall catalyst concentration is low. This could be very useful in oxygen reduction processes, such as those used in hydrogen fuel cells. Improving catalytic efficiency of a promising renewable energy source is inherently desirable, but the salen complex in question has yet to actually be made. The alkylidene chosen was shown by William Forrest in 2014 to function as a Z-selective catalyst in a different type of olefin metathesis reaction, ring-opening metathesis polymerization, but had not previously been demonstrated to be suitable for homo-coupling. Similar tungsten-monoaryloxide pyrrolide complexes have been shown to work as homo-coupling catalysts by Jiang in 2009, however. To confirm the homo-coupling catalyst of interest would work for this type of ligand metathesis, the alkylidene was first synthesized according to methods previously established by Dmitri Peryshkov in 2012 and Forrest in 2014. A series of dimerization trials were then attempted to evaluate the catalytic character of the target alkylidene. The catalyst was capable of dimerizing hexene into Z-5-decene with little to no formation of the E- regioisomer. This Zselectivity and activity is ideal for synthetic purposes, and a promising threshold for future research on the subject.

108B-U. Protocol Development for the Polymerization of BA-EGDMA-Styrene in Alkaline Solution. <u>Melanie</u> <u>Curry</u> and Susanne Striegler. *Chemistry Department, University of Arkansas, Fayetteville, AR* 72701.

Glycoproteins are bound to cellular membranes and perform functions such as cell-to-cell recognition, act as receptors for hormones and drugs, and work as structure and protection for the cell. Glycoproteins also play an integral role in the human immune system, existing as antigens and molecules of the major histocompatibility complex (MHC) which is part of the adaptive immunity. This research focuses on synthesizing micro-gel (polymer) catalysts in an attempt to modify the carbohydrates that are part of glycoproteins in order to increase their performance. Preliminary data on the elaboration of a suitable polymer system with high monomer conversion and a low polydispersity from butyl acrylate, ethylene glycol dimethylacrylate (EGDMA) and styrene monomers in alkaline solution will be discussed.

109A-U. Evaluating galactonoamidine inhibition of β galactosidase (Aspergillus oryzae) and α -glucosidase (Saccharomyces cerevisiae). Logan Mills and Susanne Striegler. Chemistry Department, University of Arkansas, Fayetteville, AR 72701.

Previous experiments have demonstrated the potential of several synthesized galactonoamidines to function as inhibitors of glycoside-hydrolyzing enzymes. These compounds resemble the structure of the complex formed by a substrate and a glycosidase during the transition state of the hydrolysis. Two different glycosidases have been chosen to advance this investigation. β -galactosidase (Aspergillus oryzae) was selected to identify the potential of these inhibitors as transition state analogues (TSAs). Additionally, α -glucosidase (Saccharomyces cerevisiae) has been selected for IC50 determinations. Preliminary data to elucidate effects of the aglycon moiety on the binding of the inhibitors to the active sites of the respective enzymes are discussed.

109B-U. Synthesis & Characterization of Pentadentate Ligands for the Formation of Binuclear Complexes. <u>Anna Doner</u> and Susanne Striegler. *Chemistry Department, University of Arkansas, Fayetteville, AR* 72701.

There is a constant need in the scientific community for efficient and selective catalysts for the hydrolysis of glycosides for applications involving glycoproteins on the cell membrane. Some of the most efficient catalysts are artificial enzyme mimics containing metal ions such as Cu(II). The purpose of this study is to synthesize two pentadentate ligands with variable intramolecular distance between the two copper ions in the ligands' corresponding binuclear complexes. The complexes will be evaluated as catalysts for the hydrolysis of glycosidic bonds in future work. A step-by-step synthesis and characterization of the pentadentate ligand 4-methyl-2,6-bis((pyridin-2-ylmethylamino)methyl)phenol) and its intermediates will be discussed here.

110A-U. Synthesis of Zirconium Phosphate Nanostructures Enhancing Proton Exchange Membrane Fuel Cell Applications. <u>Willie J. Evans IV</u>, Emily Petersen, Hulusi Turgut, Parker Cole, Z. Ryan Tian.

Chemistry Department, University of Arkansas, Fayetteville, AR 72701.

According to the previous studies, fuel cells offer clean, efficient, and renewable energy to power any device in need of a power source. In addition, fuel cells do not produce any pollution compared to gas fueled devices, such as cars, lawnmowers, etc. Utilizing Polybenzimidazole (PBI) composites in a Proton Exchange Membrane Fuel Cell (PEMFC) instead of Nafion[®], the current commercially available membrane, allows the applications of a proton conductive membrane to broaden. With these PBI ceramic composites, water can be eliminated from the system completely, unlike Nafion[®]. Eliminating sophisticated water management process from the fuel system allows fuel cell to be effectively operated at temperatures higher than 80°C. As a model membrane, pristine PBI membrane was used to establish a standard for various ceramics that are placed inside the (future) membranes. PBI and Nafion[®] membranes proton conductivity was obtained under the conditions of 100% humidity at 80°C. Results have proven PBI does not conduct protons as well as Nafion®, but with zirconium phosphate PBI will be able to compete with Nafion[®]. Ongoing research includes continuously optimizing the synthesis of zirconium phosphate and other analogs to infuse inside the membrane to test the proton conductivity and thermal stability at higher temperatures.

110B-U. The pH-triggered Conformational Dynamics of the Engineered Mechanosensitive Channel of Large Conductance. <u>Reid Shelton</u> and Mahmoud Moradi. *Chemistry Department, University of Arkansas, Fayetteville, AR* 72701.

The mechanosensitive channel of large conductance (MscL) is a homopentamer protein channel and has recently been suggested for use as a nanovalve for drug delivery. Particularly, MscL may be used in drugdelivery liposomes (DDL) containing otherwise toxic chemotherapeutic chemicals for cancer treatments. This nanovalve opens in response to membrane tension on the DDL. Consequently, toxic drugs could be released wherever a tension force is applied to the membrane. A method of delivering a drug to a more localized region is by attaching a pH-sensing label to each subunit of the homopentamer. Since the extracellular environment of a carcinogenic tumor has a lower pH compared to physiological values, the rationale behind attaching this label is sound. Ideally, the label will respond to the shift in pH and the channel will open. We are using modeling and computational methods to simulate the conformational changes of the mutated MscL. The ultimate goal is to find the open structure of the channel; the current crystal structure of tbMscL (MscL found in Mycobacterium tuberculosis) used in this work is closed. Through manipulation,

simulation and analysis of the mutated MscL, we will be able to discover how the pH-sensing label will cause a conformational shift from a closed state to an open state at a lower pH. The side effects of chemotherapy range from mild to severe in intensity. If MscL were to respond to a new stimulus, such as pH changes, chemotherapeutic drugs could be efficiently administered to a more precise location in the body.

111A-U. Response of GWALP23 Transmembrane Peptides to Incorporation of Charged Arginine Residues. <u>Karli A. Lipinski</u>, Ashley N. Martfeld, Denise V. Greathouse, Roger E. Koeppe II. *Chemistry Department, University of Arkansas, Fayetteville, AR* 727201.

Membrane proteins are essential components of many cell processes yet are understood less than soluble proteins. Charged residues, such as arginine, may contribute significantly to the function of membrane proteins. To characterize the effect of these residues on transmembrane proteins, it is useful to employ a model peptide system such as, for example, GWALP23 (acetyl-GGALW5LAL8ALALAL16ALW19LAGA-amide), a designed transmembrane peptide with interfacial tryptophan anchors. We have substituted R8 and R16 in place of L8 and L16 in GWALP23, equidistant from the center, and incorporated specific 2H-labeled alanine residues for detection by means of solid-state 2H NMR. The –R8,16 peptide folds into an alpha helical secondary structure in DLPC, DMPC, and DOPC lipid vesicles, as confirmed by circular dichroism. Solid-state 31P NMR spectra of oriented samples confirm intact bilayers in the presence of the peptide. The pattern of 2H-Ala quadrupolar splitting magnitudes along the helix indicates a significantly tilted transmembrane orientation that we currently are refining for the GWALP23-R8,16 helix in several oriented lipid membranes. Reciprocal experiments in other labs make use of double-electron-electron resonance (DEER) to measure the distance between pairs of charged functional groups similar to arginine. The combined results from complementary experimental techniques will enhance our fundamental understanding of membrane protein structure and function, helix orientation, and side-chain "snorkeling," properties which are crucial for living cells. This work will be expanded with investigations of additional peptide sequences including, for example, comparisons to the properties of the -R2,22 and -R5,19 transmembrane helices.

111B-U. Identifying the Cellular Targets of Ipomoeassin F for Cancer Therapeutics. <u>Guanghui</u> Zong, Zhijian Hu, Hazim Aljewari, Jianhong Zhou, Yuchun Du, and Wei Shi. *Departments of Chemistry and Biological Sciences, University of Arkansas, Fayetteville, AR* 72701. Ipomoeassin F, the flagship of the ipomoeassin family resin glycosides isolated from leaves of morning glory, showed potent cell growth inhibition activity with IC50 values in single-digit nanomolar range. However, its mode of action was unknown. With the long-term goal of utilizing underexploited natural glycoconjugates to study biological systems for drug development, we focus our research on development of chemical tools (activity based probe, ABP) for cellular targets identification. Several potent probes equipped with either fluorescent tag or biotin tag were obtained through efficient total synthesis and systematic SAR studies. Cell imaging studies using a confocal microscope revealed that ipomoeassin F is largely localized in endoplasmic reticulum (ER), which matches the preliminary data we obtained through SILAC-based quantitative proteomics. In addition, activity-based protein profiling is being used to verify whether ipomoeassins are covalent protein-modifiers or not. All these initial results will greatly facilitate future efforts to develop ipomoeassins as therapeutic/preventative agents or as chemical probes for basic biomedical research.

112A. Comparison of Cytokine Response to Antiinflammatory Modulators. <u>Alda Diaz Perez</u>, Tina M. Poseno, Jeannine M. Durdik, and Julie A. Stenken. *Chemistry Department, University of Arkansas, Fayetteville, AR* 72701.

Comparison of Cytokine Response to Anti-inflammatory Modulators Alda Diaz Perez1,2, Tina M Poseno2, Jeannine M Durdik1,3, Julie A Stenken1,2. 1Cell and Molecular Biology, University of Arkansas, Fayetteville, AR, United States; 2Department Chemistry and Biochemistry, University of Arkansas, Fayetteville, AR, United States; 3Department of Biological Sciences, University of Arkansas, Fayetteville, AR, United States that display different phenotypic changes in response to chemical cues (cytokines, pattern receptors, and hormones) in the microenvironment. There is a significant interest in modulating the phenotype of these cells for improved outcomes for biomaterials implants [1][2][3][4]. While there are many potential modulators to use, how they compare between in vitro outputs and in vivo outcomes is poorly understood. The objective of this study is to compare the in vitro and in vivo cytokine response from macrophages to the macrophage modulator resolvin D1 (RvD1) using cell culture and subcutaneous sponge implants. Methods: Peritoneal macrophage (PM) Cell Culture Peritoneal macrophages were extracted from the peritoneal cavity of male Sprague-Dawley rats and then the cells were centrifuged at 1100 RPM. Cells were incubated in media (which contained 15 v/v % fetal bovine serum, 1 v/v % of 100U/mL penicillin, and 84 v/v % of F-12K) for 2 hours to allow the M ϕ s to attach to the surface. M ϕ were

cultured at 5.5 x 105 cells/ mL per well. PMs were induced with lipopolysaccharide (LPS) at 50 ng/ mL, and then 5 min later, the cells were treated with RvD1 at 1 $\mu M,\,300$ nM, 100 nM, 30 nM and 10 nM and then incubated for 24 hrs. Wound fluid from sponge autoclaved polyvinyl alcohol (PVA) sponges (in 0.9 wt% NaCl) were soaked in 1 nM RvD1 for approximately 5 min, then placed subcutaneously (four sponges) into the dorsal subcutaneous space of male Sprague Dawley rats. Sponges were removed 24 hours postimplantation. Wound fluid from the sponges and supernatant from the cultured PMs were quantified for TNF- α and IL-6 using ELISA. Results and Discussion: For most of the RvD1 treatments an approximate 60% decrease in TNF- α concentration was observed after 24 hours incubation. Interestingly, RvD1 (1 µM) did not show a significant decrease in TNF- α or IL-6 concentrations compared to LPS treatment alone. RvD1; also, caused roughly a 45% decrease in TNF- $\!\alpha$ concentration in vivo in a sponge model. Predicting in vivo macrophage activation properties is not well described in the literature. This work serves as an initial step toward elucidating efficacious modulators for macrophage activation in biomaterials contexts. While the use of LPS in the cell culture experiments promotes a macrophage phenotype that would not be expected in vivo, the ability to modulate the macrophage phenotype after LPS stimulation provides a means to compare and contrast in vitro vs in vivo responses. NIH EB 014404.. References: [1] Sridharan, R., Cameron, A. R., Kelly, D. J., Kearney, C. J., & O'Brien, F. J. (2015). Biomaterial based modulation of macrophage polarization: a review and suggested design principles. Mater. Today (Oxford, U. K.), 18(6), 313-325. doi:10.1016/j.mattod.2015.01.019 [2] Spiller, K. L., Nassiri, S., Witherel, C. E., Anfang, R. R., Ng, J., Nakazawa, K. R., . . . Vunjak-Novakovic, G. (2015). Sequential delivery of immunomodulatory cytokines to facilitate the M1-to-M2 transition of macrophages and enhance vascularization of bone scaffolds. Biomaterials, 37, 194-207. doi:10.1016/j.biomaterials.2014.10.017 [3] Reeves, A. R. D., Spiller, K. L., Freytes, D. O., Vunjak-Novakovic, G., & Kaplan, D. L. (2015). Controlled release of cytokines using silk-biomaterials for macrophage polarization. Biomaterials, Ahead of Print. doi:10.1016/j.biomaterials.2015.09.027 [4] Daley, J. M., Brancato, S. K., Thomay, A. A., Reichner, J. S., & Albina, J. E. (2010). The phenotype of murine wound macrophages. J Leukoc Biol, 87(1), 59-67. Keywords: biomaterial, cell response, cytokine

112B. The structural and functional properties of a double mutant of human acidic fibroblast growth factor (hFGF-1) variant. <u>Arwa Alghanmi</u>, Srinivas Jayanthi, and Suresh K. Thallapurnam. *Chemistry Department, University of Arkansas, Fayetteville, AR 72701.*

Human acidic Fibroblast Growth Factor 1 (FGF-1), a member of the FGF superfamily, is a powerful mitogen and heparin-binding protein involved in a broad spectrum of biological processes, including angiogenesis, cell proliferation, and wound healing. Design of hFGF-1 with increased thermal stability and enhanced cell proliferation activity is highly desired for wound healing applications. We designed the variant of FGF-1 by substituting two positively charged residues in the heparin-binding pocket. The variant was overexpressed in Escherichia coli and was successfully purified to homogeneity using affinity chromatography. Far UV circular dichroism showed that the backbone conformation of the hFGF-1 did not change due to the mutations in the heparin-binding pocket. The designed hFGF-1 variant showed increased resistance to limited trypsin digestion. Results of the Isothermal Titration Calorimetry (ITC) showed that the hFGF-1 variant exhibited decreased binding affinity to heparin as compared to the wild type. 8-Anilino naphthalene 1sulfonate (ANS) binding data reveal that the introduced mutations cause a subtle change in the solventaccessible non-polar surface of the protein. These results will be discussed in detail.

113A-U. The Design and Synthesis of Novel Inhibitors of Poly(ADP-Ribose) Glycohydrolase (PARG) for Tumor-Selective Therapy. <u>Osvaldo Cossio</u>, Sreevishnu Cheerla, and Darin E. Jones. *Chemistry Department, UA Little Rock, Little Rock, AR 72204.*

The synthesis and turnover of poly(ADP-ribose) (PAR) by poly(ADP-ribose) polymerase (PARP) and poly(ADPribose) glycohydrolase (PARG) are required for normal responses to DNA damage. Genetic knockdown of PARG impairs DNA repair, sensitizes cancer cells to chemotherapeutics agents and radiation, and specifically kills BRCA-deficient breast tumors. The role of PARG activity and the mechanism explaining the requirement for PAR degradation during PARPdependent repair of DNA is unknown. We therefore initiated a medicinal chemistry program targeting PARG with small molecule inhibitors to study the effects of PAR metabolism in BRCA-deficient breast cancer cells. To study the effects of small molecule inhibitors, we synthesized a series of analogs to study the structureactivity relationship (SAR) with the protein. We analyzed and validated the synthesis of all the small molecule inhibitors synthesized in this project via 1H and 13C NMR analysis. Our future studies will involve synthesizing more small molecules that are structurally different to see how this would effect the inhibitors activity that is going to be analyzed via SAR studies in a different lab.

113B-U. Fabrication of Microcapsules for Acoustically Activated Depolymerization. <u>Kenneth Jarrett</u> and Bobak Mosadegh. Natural Sciences Department, UA Monticello, Monticello, AR 71655.

In order to help combat the risk of strokes in patients with cardiac arrhythmias, a left atrial occlusion device was designed. One particular surgical device uses microcapsules. The microcapsules developed contained one part of a two-part epoxy. The part B containing microcapsules and part A solution would be injected into a balloon-like surgical device that is used for occluding the left atrial appendage. The microcapsules that were injected into the device, when treated with ultrasound, would form an epoxy to help hold the surgical device in place.

114A-U. Determination of Fatty Acid Concentrations in Algae. Donnell White, <u>Beth Justice</u>, <u>Drake Palazzi</u>, Jessica Lester, Haley Keonig, and Andrew Williams. *Natural Sciences, UA Monticello, Monticello, AR* 71655.

Algae are of scientific and commercial interest due to their ease of culture and high fatty acid content. It is reasonable to assume that different strains of algae contain different types and concentrations of fatty acids. Of interest is the fatty acid content contained within various algal strains in the class Eustigmatophyceae. The extracted fatty acids may be of potential use for phylogenetic classification of new algal species, in addition to human consumption and producing next-generation biofuels. Algal strains were collected and isolated from Lake Chicot in Arkansas, Tower Pond and Lake Itasca at Itasca State Park in Minnesota, and Thayer Lake in the upper peninsula of Michigan. The strains collected were subjected to a 5step process for lipid preparation: lypholization, lipid extraction, filtration, esterification, and methyl ester extraction. The fatty acid extracts were analyzed using GC-MS. After qualitative determination of fatty acids by mass spectrometry, relative quantities of the fatty acids were determined by peak integration, and tricosanoic acid (C23:0) was used as a standard to determine absolute quantities. Preliminary results show differences between algal strains via relative fatty acid concentration.

114B-U. Dipeptidyl Peptidase 4 Inhibitors Augment the Activation of Cardiac Fibroblasts by SDF-1α, Neuropeptide Y, and Peptide YY. Jasmine Johnson, Delbert G. Gillespie, and Edwin K. Jackson. Chemistry/Molecular Pharmacology, UA Pine Bluff, Pine Bluff, AR 71601; University of Pittsburgh.

Dipeptidyl Peptidase 4 Inhibitors Augment the Activation of Cardiac Fibroblasts by SDF-1α, Neuropeptide Y, and Peptide YY Jasmine K. Johnson, Delbert G. Gillespie, and Edwin K. Jackson Molecular Pharmacology, SURP, University of Pittsburgh. Dipeptidyl Peptidase 4 (DPP4) inhibitors, for example sitagliptin, are a class of antidiabetic drugs that increase insulin release by blocking the metabolism of incretins, which are insulin releasing hormones. Several randomized controlled clinical trials and observational studies suggest that DPP4 inhibitors increase the risk of heart failure, although the mechanism remains unclear. We hypothesize that DPP4 inhibitors, by blocking the metabolism (inactivation) of peptides such as SDF-1 α , neuropeptide Y (NPY), and peptide YY (PYY), stimulate the proliferation of and extracellular matrix production by cardiac fibroblasts (CFs), a process that could induce cardiac fibrosis and dysfunction. To test this concept, we are investigating whether sitagliptin augments the effects of SDF-1 α , NPY, and PYY on cell proliferation (by cell counting), total collagen production (by proline incorporation), and collagen I synthesis (by ELISA) in CFs obtained from genetically hypertensive rats. The figure below summarizes results with NPY and PYY and show that both NPY and PYY augment the proliferation of CFs and that this response is enhanced by sitgliptin. Similar results were obtained with SDF-1 α . To date, the findings support our hypothesis and suggest that antagonists of SDF-1a receptors (CXCR4) or NPY/PYY receptors (Y1) could improve the clinical safety of DPP4 inhibitors.

115A-U. Phenotypic Effects of Silencing Fatty Acid Desaturase 3 in Tomato. <u>Mikiah Ballard</u>, Aravind Galla, and Fiona Goggin. *Chemistry/Entomology, UA Pine Bluff, Pine Bluff, AR 71601; University of Arkansas, Fayetteville, AR 72701.*

Fatty acid desaturase 3 (FAD3) and Fatty acid desaturase 7 (FAD7) are enzymes that are involved in fatty acid synthesis, and that are found throughout the plant kingdom. Manipulating the expression of FADs in certain plants using overexpression, antisense suppression, or null mutations has previously been shown to influence many plant phenotypes, including chlorophyll content and resistance to many stresses. For example, loss of function of FAD7 in tomato has recently been shown to immunize plants against the potato aphid, Macrosiphum euphorbiae. The goal of this study is to examine the phenotypic effects of enhancing or inhibiting expression of FAD3 in tomato. FAD3 expression levels, plant growth, and leaf number were measured in transgenic tomato lines with antisense suppression [AS line] or overexpression [OE line] of FAD3 compared to untransformed wild-type controls. These experiments allowed us to test the hypothesis that suppressing expression of FAD3 would influence plant health and immunity.

115B-U. DFT Study of the Selectivity of Monoamine Oxidase B (MAOB). <u>Samantha Jelinek</u>, Mallory Morris, Larryn W. Peterson, and Mauricio Cafiero. *Chemistry Department, Rhodes College, Memphis, TN 38112.* MAOB is an enzyme located on the outer mitochondria that is responsible for degrading penylethylamine, benzylamine, and dopamine. MAOB inhibitors are generally used as a treatment for Parkinson's disease because they stop the breakdown of dopamine. By selectively designing an inhibitor for the MAOB enzyme, the breakdown of dopamine can be reduced leading to an increase of the neurotransmitter. A suite of dopaminergic derivatives has been developed as potential inhibitors of the MAOB enzyme. The inhibitory effectiveness of these dopaminergic derivatives has been measured via in silico models in which the strength of interaction between each substrate and the enzymatic active site was analyzed. A crystal-structure of the MAOB active site, docked with the widely employed diabetes drug pioglitazone, was isolated from the Protein Data Bank (PDB ID: 4A79). The positions of novel dopaminergic derivatives were optimized in the active site using M062X/6-31G with implicit solvation and with flexible amino acid side-chains. Interaction energies between the ligands and the protein were calculated using M062X and MP2 with the 6- 311+G* basis set. At present, dopamine appears to be the strongest inhibitor of the MAOB enzyme.

116A-U. Design of novel inhibitors for the aldehyde dehydrogenases. <u>Caroline Magee</u>, Emma Selner, Larryn Peterson, and Mauricio Cafiero. *Chemistry Department, Rhodes College, Memphis, TN 38112.*

L-DOPA is commonly used as a xenobiotic for patients with conditions such as Parkinson's disease. L-DOPA is transformed into dopamine by DOPA-decarboxylase. Dopamine derived from L-DOPA is deactivated via metabolism by a series of enzymes including Aldehyde dehydrogenases (ALDH). The targeted inhibition of the ALDH enzyme may help to prolong the effectiveness of L-DOPA, resulting in a net increase in pharmacological efficiency. By selectively designing an inhibitor for ALDH, the effectiveness of the L-DOPA can be extended by regulating the metabolism of dopamine derived from L-DOPA. The effectiveness of a series of potential inhibitors has been measured via in silico models in which the strength of interaction between each substrate and the enzymatic active site was analyzed. A crystal-structure of the ALDH enzyme with an inhibitor bound in its active site (PDB ID: 4WP7) was used to create a model of the active site. Novel dopaminergic derivatives were optimized in the active site using M062X/6-31G with implicit solvation and with relaxed amino acid side-chains. Interaction energies between the ligands and the protein were calculated using MO62X with the 6-311+G* basis set. Some potential inhibitors show promising results.

116B-U. Synthesis of 6-substituted dopamine derivatives as probes of enzyme function. <u>Kendall C.</u> <u>Reed</u>, <u>Jessica A. Rogowiec</u>, Jennifer C. Rote, Mauricio Cafiero, and Larryn W. Peterson. *Chemistry Department, Rhodes College, Memphis, TN 38112.*

Dopamine is a biologically relevant neurotransmitter that plays a critical role in the human body, being involved in coordination, cognition, and the sensation of pleasure. The catecholamine core of dopamine has shown ability as a scaffold for several drugs and in other applications. Metabolism of dopamine and related catechol drugs is catalyzed by enzymes such as catechol O-methyltransferase (COMT) and sulfotransferases (SULTs). Reactions catalyzed by SULTs, for example, can increase solubility of the molecule, regulating the excretion and detoxification of xenobiotics in the human body. To further understand the function of these and related enzymes, a series of three dopamine analogues substituted at the 6-position of the catechol core is being synthesized. Progress toward the preparation of 6-iododopamine, 6-carboxydopamine, and 6acetyldopamine starting with 3,4dimethoxyphenethylamine, a commercially available material will be discussed.

117A-U. DFT Study of the Selectivity of DOPA-

decarboxylase. <u>Emily C. Harrison</u>, Abby Ritter, Larryn W. Peterson, and Mauricio Cafiero. *Chemistry Department, Rhodes College, Memphis, TN 38112.*

L-DOPA is commonly used as a xenobiotic for patients with conditions such as Parkinson's disease. Clinically administered L-DOPA is transformed into dopamine by DOPA-decarboxylase. In order to be pharmacologically effective, L-DOPA must not be metabolized before it crosses the blood brain barrier. In order to prevent premature metabolism, DOPA-decarboxylase may be inhibited in the periphery. By selectively designing an inhibitor for the DOPA-decarboxylase enzyme, the effectiveness of the L-DOPA can be extended. A suite of dopaminergic derivatives has been developed as potential inhibitors of the DOPA-decarboxylase enzyme. The inhibitory effectiveness of these dopaminergic derivatives has been measured via in silico models in which the strength of interaction between each substrate and the enzymatic active site was analyzed. A crystal-structure of the DOPA-decarboxylase active site, docked with a known DOPA-decarboxylase inhibitor, Carbidopa, was isolated from the Protein Data Bank (PDB ID: 1JS3). The positions of novel dopaminergic derivatives were optimized in the active site using M062X/6-31G with implicit solvation and with flexible amino acid side-chains. Interaction energies between the ligands and the protein were calculated using M062X and MP2 with the 6- 311+G* basis set. At present, 6-nitrodopamine appears to be an effective competitive inhibitor of the DOPA-decarboxylase enzyme.

117B-U. DFT analysis of the selectivity of known bioactive ligands in the sulfotransferase and catecholo-methyltransferase enzymes. <u>Calli Pinckney</u>, Caroline Magee, Larryn Peterson, and Mauricio Cafiero. *Chemistry Department, Rhodes College, Memphis, TN* 38112.

We have studied the substrate selectivity of a number of known bioactive ligands in sulfotransferase enzyme (SULT1A3) and catechol-o-methyltransferase (COMT) by identifying important protein-ligand interactions in the active-sites through electronic structure calculations. SULT1A3 is responsible for activating and improving the solubility of catecholamines while COMT deactivates catecholamines. Understanding how ligands behave in both of these enzymes leads to a greater understanding of the fate of dopaminergic molecules in the body. The SULT1A3 and COMT enzymes catalyze the addition of a sulfate group and a methyl group, respectively, to a variety of small molecules, including catecholaminergic molecules. Crystal structures of the SULT1A3 (PBD ID 2A3R) and COMT (PDB ID 2CL5) enzyme active sites were isolated from the Protein Data Bank. A suite of molecules with known activity in COMT were chosen from PubChem and their positions in each active site were optimized using M062X/6-31G including implicit solvation and using flexible amino acid residues. Interaction energies between the ligands and the proteins were calculated using M062X with the 6-311+G* basis set. Calculations have shown that molecules active in COMT also show a promise of strong activity in SULT1A3. In addition, a QSAR model for binding in COMT has been developed and shows promise.

118A-U. Thermodynamic Interactions of Ligands in the Tyrosinase Active Site. <u>Danielle Wilson</u>, Larryn Peterson, and Mauricio Cafiero. *Chemistry Department, Rhodes College, Memphis, TN 38112.*

We have studied the substrate selectivity of the tyrosinase enzyme by identifying important proteinligand interactions in the active-site through electronic structure calculations. Tyrosinase is involved in the conversion of tyrosine to melanin and mutation in this enzyme is the leading cause of albinism. It is also plays a key role in UV protection, detoxification, and healing. A variety of ligands analogous to known substrates of tyrosinase were chosen for study. M062X/6-31G optimization of the ligands was used to find the structures of the ligand-protein complexes in a relaxed active site with implicit solvent. Interaction energies between the ligands and the amino-acids of the activesite were calculated using MP2 and M062X with 6-311+g*; these energies can be used to determine the thermodynamic stability of the ligand in the active site. 118B-U. Design and Synthesis of Potential Inhibitors of

LpxC. <u>Rebeca Roldan</u>, <u>Lane B. Brandt</u>, Kayla A. Wilson, Gene G. Lamanilao, Maruicio Cafiero, and Larryn W. Peterson. *Chemistry Department, Rhodes College, Memphis, TN 38112*.

Potential inhibitors that mimic the natural substrate of UDP-(3-O-((R)-3-hydroxymyristoyl))-Nacetylglucosamine deacetylase, or LpxC, have been designed and synthesized. The enzyme is involved in the first committed step of the biosynthesis of Lipid A, an important part of lipopolysaccharide, which makes up the outer cell membrane of Gram-negative bacteria. When LpxC is inhibited, the production of Lipid A is halted and the virulence of the bacteria is reduced significantly. Using information found through computational study and analysis of its crystal structure, it was determined that the active site of LpxC contains three key regions: a zinc ion, a polar region, and a hydrophobic passage. The design and synthesis of analogs that include moieties that bind to the zinc and the hydrophobic region will be discussed.

119A-U. Synthesis and Characterization of Cobalt, Nickel, and Iron Schiff Base Complexes for Artificial Photosynthesis. <u>Omid Taghavi</u>, <u>Alex Graves</u>, Meghan Kiker, and Will Eckenhoff. *Chemistry Department*, *Rhodes College, Memphis, TN 38112*.

Over the next century, the world's population is expected to increase at a drastic rate; therefore it is essential to consider new and more efficient sources of energy such as the use of artificial photosynthesis to generate hydrogen gas. Hence, the development of more active and robust catalysts is necessary in order to make artificial photosynthesis a viable method of hydrogen generation. Recent studies have shown that cobalt complexes with polypyridyl groups are highly active and thus lead to a lower overpotential and higher turnover rate of hydrogen gas. Using 1,1'-(pyridine-2,6diyl)bis(2-(pyridin-2-yl)ethyl)ethan-1-imine is a promising ligand to study due to its electronic similarity to previously used ligands for cobalt catalyzed hydrogen production. However, the two pyridine substituents may act as pendant bases, enhancing its activity. Furthermore, these pendant base groups can be changed to other basic substituents, allowing for the first example of such a catalyst to be "fine-tuned" for its ligand pKa. Cobalt, nickel, and iron complexes were synthesized with this ligand and were spectroscopically and electrochemically characterized. Hydrogen production was observed under electrocatalytic conditions with the nickel and cobalt complexes.

119B-U. Binding Anti-Microbial Substrates to Zn(Tp*) Complexes. John Dewar, Arnav Thakur, and Will Eckenhoff. *Chemsitry Department, Rhodes College, Memphis, TN 38112.* The LPXC enzyme is needed for the first committed step in the biosynthesis process of cell membranes in bacteria. The active site of LPXC contains a zinc ion, which can be artificially inhibited using compounds that mimic the substrate, to prevent growth of harmful bacteria. The active site of LPXC can be modeled using ZnTp* complexes and binding of various substrates can be investigated. Zn(Tp*)Cl was synthesized to serve as the enzyme mimic. The binding of acetohydroxamate (AHA) and acetic acid (AcOH) as mimics of the drug substrates was confirmed through 1H NMR. ZnTp*AHA and ZnTp*AcO were then fully characterized by NMR and X-ray crystallography. Once a method was established to observe simple molecules, such as AHA and AcOH, complexing to ZnTp*, binding of antimicrobial substrates were carried out

120A-U. Synthesis and Characterization of Water Soluble Metallated Porphyrazines for Catalysis of Chlorine Dioxide Generation from Chlorite Ion. <u>Prince</u> <u>Aidoo</u> and Frank Hahn. *Chemistry Department, Philander Smith College, Little Rock, AR* 72202.

Porphyrazine (Pz), also known as tetraazaporphyrin has a core which is similar to the porphyrin core. Porphyrazines have been identified as an essential class of porphyrinoid macrocycles or phtalocyanine analogues, and their core is composed of pyrrole rings on which heterocyclic rings such as pyridines are directly annulated. Research indicates that chlorine dioxide (CIO2) is a better oxidizing agent than chlorine in the purification of water and pathogen decontamination since it exhibits higher antimicrobial characteristics and has a lower tendency to produce organo-chlorine byproducts which are harmful. However, large scale industrial preparation of CIO2 has health and safety concerns as it often involves the use of concentrated acids including other oxidants such as hydrogen peroxide, hypochlorite or chlorine gas. In order to investigate the feasibility of metal porphyrazines in catalyzing the generation of chlorine dioxide from chlorite ion, Iron tetra methyl 2,3-pyridino-porphyrazine (FeTM23PyPz), iron tetra methyl 3,4-pyridinoporphyrazine (FeTM34PyPz), copper tetra methyl 2,3 pyridino-porphyrazine (CuTM23PyPz) and cobalt tetra methyl 2,3-pyridino-porphyrazine (CoTM23PyPz) were successfully synthesized from commercially available urea, ammonium molybdate tetra hydrate, pyridinedicarboxylic acids, salts and methyl ptoluenesulfonate in 2-step procedures. Nuclear Magnetic Resonance (1H NMR) spectroscopy, High Resolution Mass Spectrometry (HR-MS), UV-Vis spectroscopy and Cyclic Voltammetry were used to characterize the synthesized metal porphyrazines. The experimentally measured redox potentials for FeTM34PyPz and CoTM23PyPz against Ag/AgCl reference electrode were 988.35mV and 923.70mV

respectively, which indicate that application of the metallated porphyrazines especially Iron tetra methyl 2,3-pyridino-porphyrazine (FeTM23PyPz) in substrate oxidation and chlorine dioxide generation is feasible.

120B-U. Investigating the Quantum Yield of of InP/ZnS and Gd:InP/ZnS Quantum Dots for Biological and Single-Molecule Imaging. <u>Greg Illy</u>, Matt A. Ellis, and Katye M. Fichter. *Chemistry Department, Missouri State* University, 65897.

Our lab specializes in the synthesis of nanoparticle quantum dots (QDs) for biomedical application (e.g. theronostics, single-molecule imaging, and drug delivery). These quantum dots are synthesized in coordinating organic solvents, Therefore, they must undergo a process called ligand exchange to replace hydrophobic ligands on the surface of the nanoparticles with amphiphilic ligands, allowing for the QDs to be soluble in aqueous environments. We have recently synthesized InP/ZnS QDs that have been doped with Gd in the InP core to investigate their possibility as magnetic resonance imaging agents. In this study, both InP/ZnS and Gd:InP/ZnS QDs were water-solubilized using 11-mercaptoundecanoic acid (MUA) via ligand exchange. After solubilization in water, the QDs were conjugated to an alpha-synuclein targeting peptide through a PEG linker. This alpha-synuclein targeting peptide is capable of binding Lewy bodies characteristic of Parkinson's disease. We have already demonstrated that these QDs specifically bind alpha-synuclein in neuroblastoma cells (N2a). The primary focus of this study is to compare the quantum yield (QY) of the QD fluorescence between InP/ZnS and Gd:InP/ZnS, as well as compare the QY at each step of bioconjugation. QY is very important in single-molecule imaging applications, and is measured as the ratio of photons absorbed by the QDs to photons emitted through fluorescence compared to a known standard (rhodamine 6G).

121A-U. Investigating the Effect of Selective Serotonin Reuptake Inhibitors on the Intracellular Trafficking of **5-HT1B.** <u>Meagan Rippee</u> and Katye Fichter. *Chemistry Department, Missouri State University, Springfield, MO* 65897.

The molecular basis of major depression, one of many neuropsychiatric diseases, currently remains enigmatic. Mental health is becoming more of a topic for investigators to tackle because of the growing need for people who need help to lead normal, healthy lives with their condition. The basis at which this research lies is obtaining an understanding of serotonin receptor subtype 1B (5-HT1B). This receptor has been associated with major depression, as seen in brains of patients diagnosed with unipolar depression who committed suicide. In this project, the intracellular trafficking pathways of 5-HT1B will be quantified with singlemolecule imaging, using quantum dots (QDs). In preliminary experiments typical immunocytochemistry (ICC) experiments will determine the intracellular location of 5-HT1B in N2a (neuroblastoma) cells. This information will be applied similar trials of N2a cells treated with selective serotonin reuptake inhibitors (SSRIs). In addition, the effect of these SSRIs was investigated in the presence of serotonin receptor agonists to study how the intracellular trafficking pathways of 5-HT1B are impacted by the drugs.

121B. Synthesis of highly specific quantum dot bioconjugates for single-molecule imaging in spatially confined areas. <u>Sauel P. Kasson</u>, Simona Patange, Bernice A. Agana, Vu Q. Tania, and Katye M. Fichter. *Chemistry Department, Missouri State University,* Springfield, MO 65897.

We have synthesized Quantum Dot (QD)-antibody conjugates with incredible specificity, which are uniquely suited for the demands of single-molecule imaging. We have synthesized and characterized single QD probes with different polyethylene glycol (PEG) linkers (8, 12, and 45 repeat units). These PEG linkers can then conjugate to a hydrazide that will attach to the glycosylated region of an oxidized antibody. This area of attachment is desirable to minimize interference with the Fab region of the antibody allowing for unhindered targeting. Quantitatively, we have demonstrated that non-specific binding has been limited to on average less than 1 QD per cell. Small unit PEG linkers allow for applications in spatially confined regions, and we have shown that our QD-antibody probes of shorter size (8, 12 repeat units), are equally as effective as their longer counterparts (~45 repeat units). These probes, with their highly reliable targeting and photostability, should increase the quality of data obtained though single molecule imaging with QD probes.

122A. MRI-active Gd:InP/ZnS quantum dots for diagnosis of motor neuron diseases. Jacob R. Blankenship, Matthew A. Ellis, Greg Illy, and Katye M. Fichter. *Chemistry Department, Missouri State* Unviersity, Springfield, MO 65897.

Quantum Dots (QDs) are highly fluorescent, semiconducting nanocrystals that are particularly attractive tools for a variety of biomedical applications. QDs have intense fluorescence and narrow emission bands when compared to organic fluorophores and dyes, and are closely related in size to many biomolecules, which make them good imaging tools for biomedical systems. Herein, we describe the synthesis of InP/ZnS QDs that have been doped with an MRI active metal (i.e. Gadolinium) into the crystal lattice of the QD core. This allows these QDs to be capable of multimodal imaging (fluorescence, electron, and magnetic resonance). Via the conjugation of a α - synuclein-binding peptide to the QD surface, we have observed specific targeting of α -synuclein in neural-like cells (N2a). α -synuclein aggregates are implicated in many motor neuron diseases (MNDs). Currently, these neurological diseases are very difficult, if not impossible, to clinically diagnose before death. Through specific targeting and multimodal imaging of these QDs have the potential to improve clinical diagnosis and monitor the efficacy of therapeutics for MNDs in vivo.

122B-U. Finding novel treatments for tuberculosis using deoxygenation reactions. LaShawna Hanes, Jordan Trant, and Irosha N. Nawarathne. Division of Math and Science, Lyon College, Batesville, AR 72503.

Tuberculosis, which is caused by the bacteria Mycobacterium tuberculosis, is a lung disease which kills roughly 1.5 million people a year. The most common family of antibiotics for this disease is rifamycins, which were developed 40 years ago. Rifamycins work by binding to the RNA polymerase (RNAP) and inhibiting RNA synthesis. The bacteria has since mutated in multiple ways that have decreased the effectiveness of rifamycins. Although there are many rifamycin resistant (RifR) strains of MTB, the mutations of three residues, D435V, H526Y, and S450L, account for 84% of the MTB RifR strains. Our research focused on S450L, which accounts for about 43% of the MTB RifR strains. The mutation causes the replacement of a serine amino acid with a leucine, which is both bulkier and more hydrophobic. This creates steric hindrances between the drug molecule and RNAP, allowing the bacteria to continue RNA synthesis. We are attempting to change the structure of rifamycin so it will bind to the RNAP site better. We hypothesize that we can get the desired result by removing the hydroxy on the C-8 position through chemical deoxygenation being smaller and more hydrophobic, the rifamycin analogue with the hydrogen at C-8 (after deoxygenation) will bind to the MTB RifR strains more effectively. We have used this protocol on 1-hydroxyanthra-9,10-quinone to test the reaction efficiency. Then we continued the deoxygenation at C-8 position of rifamycin S with some measure of success that will be discussed in our presentation. The deoxygenated rifamycins are tested with mutated RNAP in an in vitro transcription assay that is based on rolling circle transcription technology. This work is supported by Arkansas IDeA Network of Biomedical Research Excellence (Arkansas INBRE) and Lyon College.

123A-U. Probing Interactions of Rifamycins and Mycobacterium tuberculosis RNA Polymerases. <u>Brian</u> <u>Bumpous</u> and Irosha Nawarathne. *Division of Math and Science, Lyon College, Batesville, AR* 72503.

Tuberculosis (TB), which is caused by the bacteria Mycobacterium tuberculosis (MTB), is a lung disease

which kills roughly 1.5 million and infects over 9 million people every year. The most widely used group of antibiotics in treating TB are rifamycins. Rifamycins bind to RNA polymerase and block the RNA synthesis in MTB leading to the death of the organism. Mutations in the RNA polymerase change the polarity of the binding site and prevents the antibiotic from binding. TB evolved over the past 40 years; some strains are already resistant to many current antibiotic treatments. Among the rifamycin resistant (RifR) strains, 3 mutations, D435V, H526Y, and S450L, create 84% of all RifR strains. The mutation D435V causes the amino acid valine to replace aspartate at 435 of MTB RNAP, causing the phenylalanine side chain at F514 of the RNAP to rotate making it impossible for the acetoxy group of the rifamycin to fit into the binding site due to sterics. We hypothesize that by removing the acetoxy group (-OAc) and leaving behind a hydroxy group (OH) at the C-25 position (to better attract the D435V), rifamycin will bind better to RNAP of RifR strains. We are in the process of testing the developed modified rifamycins using rolling circle transcription assay. This work has been supported by Arkansas IDeA Network of Biomedical Research Excellence (Arkansas INBRE) and Lyon College.

123B-U. Development of Fluorinated Rifamycin Derivatives. <u>Gareth Stout</u> and Irosha Nawarathne. Division of Math and Science, Lyon College, Batesville, AR 72503.

Tuberculosis (TB) has been treated effectively for the last 40 years. However, it is beginning to mutate causing drugs to become less effective. In order to combat the adaptions made by TB causing bacteria, Mycobacterium tuberculosis, we propose a structural change to drugs in rifamycin family that are used in TB treatment to improve their drug efficacies. Our plan is to replace the C8 hydroxyl group of rifamycin derivatives with fluorine engaging organic synthetic strategies. Then we will analyze the effectiveness of the modified drugs via in vitro transcription assays. These fluorine-incorporated rifamycins will also be developed as an imaging agent to facilitate diagnosis through TB screening, thus promoting prevention and/or early treatment of the disease. This work is supported by Arkansas IDeA Network of Biomedical Research Excellence (Arkansas INBRE) and Lyon College.

124A-U. Effect of mitochondrial CYP2E1 overexpression on mitochondrial biogenesis in HepG2 cells. Andres Car, <u>John Anderson</u>, and Grover Miller. *Chemistry Department, Hendrix College, Conway, AR* 72032.

Chronic alcohol induces induces hepatic oxidative stress, characterized by increased concentration of reactive oxygen species. Cytochrome P450 2E1 (CYP2E1, both microsomal and mitochondrial) contribute to this increased oxidative stress. Chronic alcohol also induces the expression of mitochondrial biogenesis genes as a compensatory mechanism against mitochondrial oxidative damage. The mechanisms by which chronic alcohol induces mitochondrial biogenesis genes are unclear. In this work, we evaluated the hypothesis that mitochondrial reactive oxygen species derived from mitochondrial CYP2E1 trigger the induction of mitochondrial biogenesis genes in hepatocytes. HepG2 cells overexpressing mitochondrial CYP2E1 (mE10 cells, transfected with an expression vector containing the human CYP2E1 cDNA lacking the coding sequence for amino acids 2-34) and HepG2 cells not expressing any cytochrome P450 (C34 cells, transfected with an empty expression vector) were used in this study. Overexpression of mitochondrial CYP2E1 in mE10 cells was confirmed by western blot, RT-PCR and enzymatic analysis. Overexpression of mitochondrial CYP2E1 in HepG2 cells occurred together with increased mitochondrial reactive oxygen species evaluated by flow cytometry using MitoSox Red and by electron paramagnetic resonance spectrometry using Mito-Tempo-H. mE10 cells showed higher expression at the mRNA level of the mitochondrial biogenesis genes TFAM and NRF1, together with increased mitochondrial mass evaluated by flow cytometry using MitoTracker Green. These results show a correlation between mitochondrial CYP2E1 expression, mitochondrial oxidative stress, and expression of mitochondrial biogenesis genes. The mechanism by which mitochondrial CYP2E1 induces mitochondrial biogenesis is under further investigation in our lab.

124B-U. Intentional mistakes: Synthesis and Evaluation of Tautomerically Ambiguous Nucleosides as Potential Antiviral Agents. <u>Wendy Fernandez</u>, Shannon M. Hardage, Carlie M. Clem, Sarah E. Kuhn, and Vincent K. Dunlap. *Chemistry Department*, *Henderson State University, Arkadelphia, AR 71999*.

Viral infections are a severe issue that greatly affects our society. In particular, the human immunodeficiency virus (HIV) creates a rather challenging problem for medical experts. HIV is able to avoid prophylaxis due to its highly mutagenic nature. Although research for HIV treatment in this area has been successful, the therapies currently used come with harsh side effects for the patients. This issue demands development of more effective HIV treatments with less severe side effects. Our research focuses on one of these developments. We have synthesized a set of nucleosides with ambiguous hydrogen bonding faces that when incorporated into the viral DNA, will destabilize the DNA. A combination of such incorporation and the high error rate of the polymerase enzymes of the HIV virus may lead to an error catastrophe within the HIV genome causing DNA ablation of the HIV virus. Presented here

are the results of the synthesis and thermal denaturation of DNA duplexes containing the described nucleosides.

125A-U. Optimization of the Click Reaction and the Sonogashira Coupling Reaction for Bioorthogonal Chemistry. <u>Carlie Clem</u> and Wei Shi. *Chemistry* Department, Henderson State University, Arkadelphia, AR 71999; University of Arkansas, Fayetteville, AR 72701.

Gaining a better understanding of the mode of action of a drug is highly beneficial for achieving its medicinal potential safely. The Shi lab is studying the potency of ipomoeassin F, a natural product found in morning glories. The compound is not found in abundance in nature, so it is being synthesized and functionalized in the lab to create a viable cancer drug. A chemical proteomics approached termed activity-based protein profiling is being adopted for identifying protein targets of Ipomoeassin F. It involves a critical bioorthogonal step for protein detection and purification, which is the focus of this research project. The chosen bioorthogonal reactions to be researched are a click reaction and the Sonogashira coupling reaction. The click reaction being studied is a copper catalyzed azide-alkyne 1,3-dipolar cycloaddition. The Sonogashira coupling reaction couples a terminal alkyne with and aryl or vinyl halide and is reacted with an amine base using a copper catalyst and a palladium catalyst. This research is still in its early stages as to determine what bioorthogonal reaction has the most optimal conditions for probing biological systems. An area that has not been previously studied by the Shi lab and is an area of emphasis in this project is the kinetics of these reactions.

125B-U. Math Anxiety and Cortisol as a Biomarker. <u>Mary Davis</u>, Colton Lechak, and David Bateman. *Chemistry Departmetn, Henderson State University, Arkadelphia, AR* 71999.

Generalized test anxiety and math anxiety are documented disorders that are especially prevalent amongst college students. College algebra has been proven to be the class most indicative of continued success in college, and by extension success in science, technology, engineering, and mathematic (STEM) career fields. The demand for STEM graduates is at an all-time high and is only continuing to increase, so it is necessary to both produce and retain STEM majors in their respective programs. The purpose of this study is to quantify math test anxiety in students enrolled in intermediate algebra courses and to formulate different coping, studying, and teaching methods in order to improve student performance and reduce stress levels in order to increase student persistence in STEM degree tracks. Many methods to alleviate student test anxiety have been proposed, but no studies exist that connect

the proposed methods to their effectiveness as measured by biological assays. Such studies could serve as a monumental gauge of methods intended to assuage student math and test anxiety. From saliva collected from the students at chosen intervals, cortisol levels were measured and used as a stress biomarker through the implementation of an enzyme-linked immunosorbent assay (ELISA). Our initial analyses are indicative that cortisol levels are heightened after the subjects attend the intermediate algebra class, which does agree with the hypothesis initially postulated. Further study will need to be conducted in order to confirm the results initially derived, but early outcomes are promising.

126A-U. Synthesis of a DMT Molecule to Improve the Selectivity of Phosphine Addition in RNA. <u>Andrew</u> <u>Hodge</u> and Vincent Dunlap. *Chemistry Department, Henderson State University, Arkadelphia, AR* 71999.

The synthesis of DNA in a laboratory setting is a welldocumented and efficient synthetic process. However, due to RNA's additional hydroxyl group in the 3' position, the synthesis of RNA leads to inefficiency during phosphite addition. The 5' position on both DNA and RNA can be protected, and in DNA only the 2' hydroxyl is available for phosphite addition, but in RNA the selectivity between 2' and 3' hydroxyl is difficult to predict. Through a structural analog of the 5' hydroxyl protecting group, a molecule is being designed and synthesized which will coordinate with the 3' position causing both the 5' and 3' hydroxyl groups to be protected. This will hopefully lead to a more selective process during phosphite addition, thus increasing yields in RNA synthesis. Presented here will be the synthetic aspects of the project.

126B-U. Collection, Separation, and Assay of a Fat Mobilizing Substance. Dennis Province, Cindy White, Lance Benson, and Madison Everett. *Chemistry* Department, Harding University, Search, AR 72143.

FMS (fat mobilizing substance), a protein thought to be produced by the body in response to fasting, induces an accelerated rate of lipolysis and ketosis in order to substitute for the reduced caloric intake. While previous research has been done to identify the effects of FMS via injection into rodents and measuring loss of carcass fat, this study seeks to isolate FMS from the urine of human patients who have undergone the fasting process, initiating the production of the protein. For this research, we isolated crude FMS from urine through gel filtration, ion-exchange chromatography, and HPLC. The resultant purified protein was added to adipocytes to test for fat-mobilizing activity. Several fractions were identified to induce fat-mobilizing activity. We plan to sequence and analyze these fractions via bioinformatic methods. Determining the protein sequence could aid in

future studies seeking to induce fat mobilizing activity without submitting subjects to a fasting state. Conversely, isolation of FMS can aid in treatment of patients suffering with lipodystrophy.

127A-U. Identifying the Structure of Fat Mobilizing Substance (FMS-1) Associated with Congenital Lipodystrophy. <u>Mallory Bryant</u> and Dennis Province. *Chemistry Department, Harding University, Searcy, AR* 72143.

A fat mobilizing substance is present in the urine of fasting individuals. It is believed that the same fat mobilizing substance is found in the urine of people who suffer from congenital lipodystrophy. A sample of urine from an individual with congenital lipodystrophy was obtained and purified. It was separated into fractions using size exclusion chromatography. For future research, the sample will be further purified through ion exchange chromatography along with being examined through gel electrophoresis and mass spectrometry. The results will be compared with data from samples obtained from a healthy fasting individual and a healthy non-fasting individual processed using the same protocol.

127B-U. Pharmaceuticals and Personal Care Products Found in Gin Creek, Searcy, AR. John Rich and Edmond Wilson. Chemistry Department, Harding University, Searcy, AR 72143.

Gin Creek, in Searcy, Arkansas, is the primary drain for run-off water from the town. An analysis of the water in Gin Creek is being carried with particular emphasis given to detection of PPCPs (Pharmaceuticals and Personal Care Products) in the stream. The analytical procedure involves collecting water samples at key points of the creek. The organics in the water are extracted with methylene chloride which is then concentrated by means of a rotary evaporator and subjected to analysis by gas chromatography using a quadrupole mass spectrometer as the detector (GM/MS). The results of these analyses are presented.

128A-U. Sterilization of aqueous solutions using a novel solar energy powered device. Mariusz P. Gajewski, <u>David Williams</u>, and <u>Justin Baarrett</u>. *Physical Sciences, Arkansas Tech University, Russellville, AR 72801.*

The research described here focuses on a prototype of a device designed as a solar powered tool useful in sterilization of water (or solutions) contaminated by microorganisms. The device has potential applications in biomedical field where sterile solutions or drinkable water are required, but where other means are not available or impractical. The method of sterilization described here is based on photoactivatable porphyrins

covalently anchored to a solid support. There are several known catalysts based on transition metal oxides capable of performing this function; however, such systems possess several drawbacks: their toxicity, price, light absorption inefficiency and, if photosensitized, their lack of stability. All of these undesired properties render such systems unsuitable in the biomedical field. Porphyrins are remarkably efficient light absorbers throughout (practically) entire visible spectrum, which makes them very attractive targets for the abovementioned applications. Linking them covalently to a solid support dramatically increases the system's stability. Additionally, due to porphyrins spectral properties in visible region, there is no need for expensive UV permeable quartz equipment. The device design and construction (animated) as well as application and efficiency in process of photodecontamination utilizing standardized samples of E. coli contaminated water are presented and preliminary results are discussed.

128B-U. Comparative sulfur oxidation genomics in Halothiobacillus neapolitanus. <u>Fy'nisha Oliver</u>, Jennifer Branch, and Newton Hilliard. *Physical Sciences*, Arkansas Tech University, Russellville, AR 72801.

Genomic analysis of sulfur oxidizing genes in the obligate aerobic chemolithoautotrophic purple sulfur bacterium Halothiobacillus neapolitanus indicate the presence of a hybrid, yet incomplete, set of pathways for complete sulfur oxidation. The presence of a sulfur oxygenase reductase (sor) gene for oxidation of elemental sulfur to sulfite has been verified. This gene is more commonly found in archaea species. Genes for oxidation of sulfide include both multiple versions of sulfide: guinone reductases (sgr) similar to those found in anaerobic phototrophic green and purple sulfur bacteria (GSB and PSB respectively) and a presumably cytochrome linked sulfide dehydrogenase (sdh) similar to that found in proteobacteria species. Genes for the oxidation of partially oxidized sulfur compounds such as thiosulfate include the majority of genes for a thiosulfate oxidizing multienzyme system (TOMES) type pathway. The major missing piece for this pathway is a soxK gene which in the GSB and PSB result in accumulation of cell associated polythionates. In addition to the TOMES pathway, genes for a putatively heterodimeric tetrathionate forming thiosulfate dehydrogenase (tdh) have been identified. The apparently obligate heterodimeric nature of this enzyme is unique compared to other species with this same activity due to the presence of the ATGA coexpression motif within the overlapping reading frames. In addition, this species apparently lacks genes for a tetrathionate hydrolase capable of processing the product of thiosulfate dehydrogenase potentially explaining reports of accumulated 'sulfur' under certain growth conditions. These findings explain observed

patterns in Ht. neapolitanus growth on different sulfur containing substrates.

129A-U. Binary Liquid-vapor Phase Diagrams with Desktop Gas Chromatography. <u>Paul Charles Bayliss</u> and Bradley A. Rowland. *Chemistry Department, Henderson State University, Arkadelphia, AR* 71999.

In this study, a new technique for obtaining binary liquid-vapor phase diagrams for Physical Chemistry Laboratory is proposed. An apparatus similar to that of J. McCormick from the University of Kansas was devised to collect both liquid and vapor fractions at several different compositions. This technique, however, differs in that there is no reliance upon refractometry to determine the composition of the liquid and vapor phases. Rather, Vernier's tabletop Gas Chromatograph is utilized to quickly resolve the composition of the phases. The results of an acetone/cyclohexane mixture are presented as well as the results of an azeotropic mixture.

129B-U. Utilization of Numeric Analytical Continuation to Study Node Evolution in the Sech Wave Packet. <u>Wade Garrett</u> and Bradley A. Rowland. *Chemistry Department, Henderson State University, Arkadelphia, AR* 71999.

In this study, the free-evolving Sech wave packet and its node development are explored. Numerical Analytic Continuation (NAC) is utilized to visualize the develoment and healing of nodes in the evolving wave packet on the real axis.

130A-U. Few-layered, Nanosized Tungsten (IV) Disulfide Antioxidant and Its ROS Scavenging Abilities. <u>Neden Yacine</u>, Bushra Ergul, and Wei Zhao. *Chemistry Department, UA Little Rock, Little Rock, AR 72204.*

Two dimensional layered nanomaterials have sparked great interest in whether they possess antioxidant abilities that may be comparable to the natural antioxidants vitamin C, vitamin E, etc. Few-layered, nanosized tungsten (IV) disulfide is the compound of interest. Here we use a sensitive near infrared probe, single-walled carbon nanotubes (SWNTs) to determine if the nanocompound, prepared by a mild sonication process, possesses antioxidant abilities which can scavenge reactive oxygen species (ROS). The ROS scavenging behavior of the nanocompound is analyzed by measuring the magnitude of spectral recovery of the hydrogen peroxide-suppressed SWNT suspensions. The nanocompound is first purified by a centrifuge and wash process. Concentration-dependent reactions are conducted in order to examine how the concentration of the few-layered nanocompound plays a role in the spectral recovery. Further discussion includes an analysis of the spectral data of the nano compound.

Physics

Friday Oral Platform Session

ORAL – 3:20. Photoelectrical Characterization of Bacteriorhodopsin suspended in a lipid bilayer membrane. <u>Orion Guan</u>, Joel Kamwa, and Jiali Li. Physics Department, Truman State University, Kirksville, MO 63501.

Bacteriorhodopsin is a protein that acts as a light-driven proton pump when embedded in a lipid bilayer membrane. We report our efforts to incorporate bacteriorhodopsin into bilayer lipid membranes using a method that would be easy to apply to multiple apertures at once, with consistency. When these membranes were tested for their resistance and capacitance as signs of their quality, membranes created with the same method at different times were found to have capacitance on the order of picofarads and a resistance that is constantly .3 $G\Omega$ for an aperture of 163 μm in diameter. A 532 nm laser was used at these membranes to activate the bacteriorhodopsin proteins to create a proton gradient, measured as photocurrent across the membrane. We discuss possible reasons that the attempts to detect photocurrent have been largely unsuccessful in spite of multiple changes and variations made to the procedure over the course of the experiments.

ORAL – 3:35. Ultrasonic bone assessment using backscatter power difference technique. <u>Luke</u> <u>Fairbanks</u> and Brent Hoffmeister. *Physics Department, Rhodes College, Memphis, TN 38112.*

Osteoporosis is a bone disease which disrupts the balance of cell destruction and new cell construction within bone. This decay leads to increased porosity within the bone tissue and heightened fracture risk. The focus of our research is the diagnosis of the bone disease osteoporosis with ultrasound. Methods: An ultrasonic wave centered around 3.5 MHz is sent into 55 cubic bone specimens taken from the porous interior of 14 donated femurs. The sound waves echo off of the bone, one device both sends and listens to the signal. The signal which is analyzed, the echo, is referred to as backscatter. The characteristics of the decay of the signal reveal the mechanical properties, mainly density, of the bone. The normalized mean backscatter difference(nMBD) is determined by attaining the mean power difference between two gated portions of the signal and dividing by the center to center separation between the gates. nMBD was calculated for 21 different choices of gate location, duration, and separation. Results: The difference spectrum changes when the time segments, the gates, change. nMBD

demonstrated strong linear correlations with measured bone density ($0.73 \le R \le 0.90$) depending on gate choice. Greater correlations were observed as the combined values of gate width and gate separation increased. Conclusion: nMBD may be sensitive to the changes in bone caused by osteoporosis. The correlation of nMBD with bone density depends on gate choice.

ORAL – 3:50. Anisotropic Differential Reflectance Spectroscopy of Thin GeSe. Joseph Matson¹, Grace Woods², and Hugh Churchill³. ¹Physics Department, Hendrix College, Conway, AR 72032, ²UC Santa Cruz, Santa Cruz, CA 95064, ³Physics Department, University of Arkansas, Fayetteville, AR 72701.

Atomically thin monochalcogenides are predicted to exhibit a two-dimensional structural phase transition. This phase transition could be useful for designing new phase change memory devices. The critical temperature is dependent on the material as well as the thickness, and is predicted to occur just above room temperature for monolayer GeSe. We used differential reflectance spectroscopy on thin samples of GeSe to measure changes in the optical anisotropy with temperature as a signature of this phase transition. We constructed an apparatus for temperature-depedendent spectroscopy of micro-scale GeSe samples, and measured anisotropic optical absorption of thin GeSe. We observed a decrease in optical anisotropy of GeSe at elevated temperatures, which may be a first indication of the continuous transition from a rectangular to a square lattice in that material. This work was supported by NSF REU Grant #EEC-1359306.

ORAL - 4:05. Suppression of Radiation-Induced Chromosome Damage by GT3 and the Role of Microgravity. Taylor Burdick, Abdel Bachri, Rupak Pathak, Sanchita P. Ghosh, Igor Koturbash, Marjan Boerma, Regina K. Binz, Jeffrey R. Sawyer, and Martin Hauer-Jensen. Engineering and Physics, Southern Arkansas University, Magnolia, AR 71753. Ionizing radiation, such as outer space radiation, generates reactive oxygen species (ROS), which cause DNA double-strand breaks (DSBs) that are responsible for cytogenetic alterations originating from Chromosome damage. Because antioxidants are potent ROS scavengers, we investigated whether the vitamin E y-tocotrienol (GT3), a radio-protective multifunctional dietary antioxidant, can suppress radiation-induced cytogenetic damage. We measured DSB formation in irradiated primary human umbilical vein endothelial cells (HUVECs) by quantifying the formation of y-H2AX foci. Chromosomal aberrations (CAs) were analyzed in irradiated HUVECs and in the bone marrow cells of irradiated mice by conventional and fluorescence-based chromosome painting techniques. We found that GT3 pretreatment reduced DSB formation in HUVECS, and decreased chromosome aberration in HUVECs and

mouse bone marrow cells after irradiation. Moreover, GT3 increased expression of the DNA-repair gene RAD50 and attenuated radiation-induced RAD50 suppression. We conclude that GT3 attenuates radiation-induced cytogenetic damage, possibly by affecting RAD50 expression. GT3 should be explored as a therapeutic supplement to reduce the risk of developing genetic diseases after radiation exposure. Finally, the effect of outer space radiation exposure and near-zero space gravity environment on DNA damage is not well documented, and is a primary concern to NASA in furthering its goal for deep space exploration. We illustrate technics of subjecting the cells to microgravity and discuss our preliminary findings on the role of microgravity.

ORAL – 4:20. Molecular Dynamics Simulations of the Mechanical and Structural Prosperities of Silica and Aluminosilica Mesoporous Materials. Jesse

<u>Underwood</u>, Dayton G. Kizzire, J. Thomas, R. Sakidja, and R.A. Mayanovic. *Physics, Astronomy, and Material Science, Missouri State University, Springfield, MO* 65897.

The high surface-to-volume ratio and nano-scale pores provide excellent potential for biomass gasification and heterogeneous catalysis applications of periodic mesoporous materials. The goal of this study is to investigate the relationship between the composition (i.e., silica vs aluminosilica) and the mechanical properties of mesoporous materials having consistent pore structure. A series of molecular dynamics (MD) simulations were used to investigate the mechanical and structural properties of bulk and mesoporous silica and aluminosilica materials. In case of porous materials, the MD simulations were made for simulation cells containing a two-dimensional hexagonal SBA-15 pore structure for the mesoporous silica and aluminosilica. The MD simulations were executed using LAMMPS software on the Stampede supercomputer. Varying values of hydrostatic pressure were applied to either system until an equilibrium volume was obtained; the change in volume vs change in pressure was used to determine the bulk modulus. The process was repeated for various porosity values of the mesoporous systems. Both the mesoporous silica and aluminosilica obey an exponential reduction of the bulk modulus with increasing percent porosity. We find that the simulated mesoporous SBA-15 type silica exhibits slightly weaker mechanical properties than either 14.5 or 33 cation percentage Al SBA-15 type aluminosilica. Bond angle analysis using General Utility Lattice Program (GULP) was made to ascertain the structural properties of the simulated mesoporous silica and aluminosilica at the atomic level.

ORAL – 4:35. The Indeterminate Case of Classical Static Friction when Coupled with Tension. Jacob Russell and Kenneth Hahn, Engineering Department, John Brown University, Siloam Springs, AR 72761.

The mass on an inclined plane held in static equilibrium by both static friction and tension provides an interesting case of indeterminacy in classical mechanics. We present both theoretical analysis and experimental evidence which demonstrate that the static friction force may assume any value allowed by the inequality f(static) < u[•] F(normal) and the balance of other forces. In fact, at any angle of inclination, friction may assume its maximum, its minimum or even a zero value when working in cooperation or competition with tension.

Physics

A and B – Saturday 8:00 – 10:15 Posters

(Posters designated "U" will be judged.)

201A. Development of Many-body Potentials for Al-TiN nanolayered composites. <u>Paul Simanjuntak</u>, Ridwan Sakidja, and Caizhi Zhou. *Physics, Astronomy, and Materials Science, Missouri State University, Springfield, MO* 65897.

We are developing an interatomic potential that is suitable for the ternary system of Al-TiN. The ternary system has garnered a great interest especially due to the potential use of Al-TiN nanolayered composites. Previous works have primarily concentrated solely on the binary systems of Al-Ti and Ti-N by using the Embedded Atom Model (EAM) or Modified Embedded Atom Model (MEAM) and so far, there has been no potential development work reported on the more complex ternary system. We employed the force-fitting code Potfit and the large sampling of force, stress & energy calculation results from the ab-initio molecular dynamics simulations (as implemented in VASP) to optimize the analytical forms of the many-body potentials. The deformation behavior of the nanolayered composites will be further assessed through the classic molecular dynamics simulations and discrete dislocation dynamics method.

201B. Experimental and Modeling Study of Vibrations in Functionalized Carbon Materials. <u>Neva</u> Agarwala, Ridwan Sakidja, and Maria Stepanova. *Physics, Astronomy, and Materials Science, Missouri State University, Springfield, MO* 65897.

Raman spectroscopy is an important tool to characterize vibrational dynamics of carbon materials. In this study, molecular vibrations in graphene oxide (GO) and several other carbon materials were investigated both experimentally and computationally using Density-

Functional Theory (DFT) calculation. Raman spectra of aqueous solutions of GO and fullerenol (C60(OH)n) were acquired with a Horiba LabRAM instrument using a 532 nm excitation wavelength. Using the Quantum Espresso DFT code, Raman bands of several structures of oxidized graphene were also calculated. The models consisted of a hexagonal in-plane structure of graphene with various numbers and positions of hydroxyl, carbonyl, and epoxy groups predominantly on the basal plane, representing different oxidation levels. Various types of defects were introduced into the GO models by replacing one C atom with an O atom to accommodate more carbonyl groups. OH, C–C, and other vibration modes in the Raman spectra have been identified for different models and compared with the experimental data, as well as with the predicted Raman bands of CH4 and CO2 molecules. Substantial differences of Raman bands between CH4 and CO2 molecules and GO have been demonstrated. Keywords: Graphene, Graphene oxide (GO), Raman spectrum, DFT calculations.

202A. Tungsten Oxide Thin Films Fabricated using Femtosecond and Nanosecond Pulsed Laser

Deposition. <u>Anthony Pelton</u>, Hayley Sohn, and Robert Mayanovic. *Physics, Astronomy, and Materials Science, Missouri State University, Springfield, MO* 65897.

Pulsed laser deposition (PLD) is a promising technique for creating inexpensive, nanostructured thin films which may be suitable for photocatalysis. During the course of our study we have prepared tungsten oxide thin films by using two types of PLD techniques. The first method is carried out at US Photonics, Springfield, Mo, using a femtosecond laser while the second method relies on an excimer (nanosecond) laser which is located at Missouri State University. The PLD films were deposited on glass and silicon substrates. After deposition the thin films were annealed to 450 °C up to 30 hours in air. Characterization of the films' structure and morphology was made using SEM, XRD, Raman Spectroscopy, and XPS, both before and after annealing. Prior to annealing the films made using the femtosecond PLD (f-PLD) are rougher and display more texture than the films grown using nanosecond PLD (n-PLD). Before annealing the f-PLD films exhibit both 3-D nano-crystalline and amorphous structures, whereas the n-PLD films are predominately amorphous before annealing. Our results from the characterizations described above will be discussed.

202B. Synthesis and Characterization of NiO@NixMn1-

xO Core-Shell Nanoparticles. <u>Samiul Hasan</u> and Robert A. Mayanovic. *Physics, Astronomy, and Materials Science, Missouri State University, Springfield, MO* 65897.

Inverse core-shell nanoparticles, comprised of an antiferromagnetic (AFM) core covered by a

ferromagnetic (FM) or ferrimagnetic (FiM) shell, are of current interest due to the tunability of their magnetic properties. NiO is typically antiferromagnetic in nature and has a Neel temperature of 523 K. Our primary objective in this project is to synthesize and characterize core-shell nanoparticles (CSNs) comprised of a NiO (AFM) core and a shell consisting of a Mn-NiO (FM/FiM) compound. The synthesis of the CSNs was made using a two-step process. The NiO nanoparticles were synthesized using a chemical reaction method. Subsequently, the NiO nanoparticles were used to grow the NiO@NixMn1-xO CSNs using our hydrothermal nanophase epitaxy method. XRD structural characterization shows that the NiO@NixMn1-xO CSNs have the rock salt cubic structure throughout. Magnetic measurements made using a SQUID show that the CSNs exhibit AFM/FM characteristics with a coercivity field of 425 Oe at 5K. The field cooled vs zero field cooled hysteresis loop measurements show a significant exchange bias effect between the AFM core and FM shell of the CSNs. Further details of our measurements and synthesis of our CSNs will be presented.

203A. Investigation of Iron Ion Transit in Ferritin by Molecular Dynamics Simulations. <u>Shah Alam Limon</u> and Maria Stepanova. *Physics, Astronomy, and Materials Science, Missouri State University, Springfield, MO* 65897.

Ferritin is a ubiquitous intracellular iron-storage protein with an ability to uptake, mineralize and release iron in a controllable manner. This protein is composed of 24 subunits forming a globular shell allowing for storage of mineralized iron, with several channels responsible for the transit of ions into the shell and out of it. Understanding of the detailed molecular functioning of ferritin is important for rational design of biomimetic conjugate nano-biosystems containing ferritin-like components. The goal of this work is to understand the details of iron ions transit through pertinent channels in the ferritin shell. Three subunits forming an iron ion transit channel from the 24-fold shell (PDB ID: 5CZU) were subjected to molecular dynamics (MD) simulations in water using the Gromacs 5.1.1 software with an OPLS-AA force field. Nine ions (Fe2+) were added to the system, and transit of the ions through the channel was investigated. The molecular mechanisms involved in the ion transit, as observed in our MD simulations, are expected to be representative of the iron uptake and release processes that occur in the ferritin globule.

203B. Synthesis and Characterization of Copper and Aluminum based Chromium Oxide Core-shell Nanoparticles. <u>Tamzid Ibn Minhai</u>, M.D. Hossain, M.

Benamara, and R.A. Mayanovic. *Physics, Astronomy, and Materials Science, Missouri State University, Springfield, MO* 65897.

Modified chromium oxide nanoparticles are regarded by scientific community as one of the most promising class of nanomaterials for applications in spintronic devices, catalysis, magnetic device applications and biomedical affairs. In the course of present study, chromium oxide based core shell nanoparticles were synthesized by a combination of chemical and hydrothermal methods using a two-step process. In this process we have been successful in formation of nano phase Cu and Al based shell over a Cr2O3 core nano phase. Our characterization shows CSNs formation with Cu and Al being predominantly distributed in shell region. The CSNs were characterized using XRD, EDS, SEM, XPS, TEM and SQUID magnetometry. The Cr2O3@CuxCr2-xO3 and Cr2O3@AlxCr2-xO3 have sizes of 36.5 nm and 37.5 nm respectively. The magnetic measurements have shown predominantly antiferromagnetic (AFM) behavior with some exchange bias field value of 163 Oe and 455 Oe for Cr2O3@CuxCr2-xO3 and Cr2O3@AlxCr2-xO3, respectively.

204A-U. Development of solid-state super ionic electrolyte for electrochromic applications. <u>Thomas</u> <u>Callaway</u> and Saibal Mitra. *Physics, Astronomy, and Materials Science, Missouri State University, Springfield, MO* 65897.

In this project, we report the development of a lithium ion-based solid-state electrolyte for electrochromic devices. An electrochromic device changes color reversibly and has great potential as an energy saving device. The device consists of two FTO-coated glass, which act as contacts. Tungsten oxide films were also deposited on one of the FTO contacts. We report the deposition of xLi2SO4-(1-x)(Li2O-P2O5) thin films on glass substrates using electron beam evaporation and tungsten oxide films using puled laser deposition. The electrolyte provides the lithium ions for migration into the tungsten oxide films. The performance of these lithium-based electrolytes will be discussed.

204B. Diffusion Behavior of Lithium in LiPO3 and LI3PO4 model systems. <u>Md Shafiqul</u> Islam, Ridwan Sakidja, and Saibal Mitra. *Physics, Astronomy, and Materials Science, Missouri State University, Springfield, MO* 65897.

The use of the Li cation and an understanding of it's behavior is central to development of modern charge storage devices such as the Li-ion batteries. In the current study, we have investigated the diffusion of Liion in two model systems for Li-ion compounds, namely lithium phosphite (LiPO3) and lithium phosphate (Li3PO4). For this purpose, we have performed Density Functional Theory (DFT) calculations on the various diffusion pathways from different possible vacancy sites within the two crystal structures. We calculated the activation energy barrier for the various diffusion modes by using the nudge elastic band (NEB) method as implemented in Quantum Espresso DFT code. We then seek to correlate these diffusion characteristics to the results of neutron scattering experiments to further understand the Li ion hopping mechanisms in a more complex structure such as 0.6Li2SO4 -0.4(Li2O-P2O5) amorphous electrolyte.

205A. Growth and Characterization of Single Phase Iron Nitride Thin film using Pulsed Laser Deposition. Ahmed Rayhan Mahbub and Mahmud Reaz. Physics, Astronomy and Materials Science, Missouri State University, Springfield, MO 65897.

Iron nitride thin films have been important magnetic materials for the past few decades due to its potential applications significantly in the magneto-electronics. Biggest challenge of any nitride films is the growth of single phase nitride films on a substrate. In this work, iron nitride films are grown using reactive pulsed laser deposition on a silicon substrate. The purpose is to optimize single phase Fe3N. The optimization has been done by changing the growth parameters in the pulsed laser deposition such as the gas mixture and substrate temperature. The composition, structure and surface parameters are characterized by X-Ray Diffraction, Raman spectroscopy, and scanning electron microscopy. The magnetic properties of the nitride film have been characterized using superconducting quantum interference magnetometer and ferromagnetic resonance spectroscopy. The detailed analysis of the characterized results will be discussed in this presentation.

205B. Synthesis and Characterization of Tunable Magnetic Luminescence Zno-Iron Oxide Core-Shell Nanoparticle. <u>Mahmud Reas</u> and Kartik Ghosh. *Physics, Astronomy and Materials Science, Missouri State* University, Springfield, MO 65897.

Core-shell nanoparticles have attracted considerable interest for its multifunctional properties. At the same time, oxide materials have been investigated due to its tunable properties and structures with high electron correlation. In this project, we exploited the ZnO luminescence and the adjustable magnetic properties of iron oxide. ZnO-Iron oxide core-shell nanoparticles has been developed using physiochemical method. Magnetic properties of the nanoparticle have been successfully varied while keeping the luminescence intact. Characterizations using SQUID, SEM, TEM, RAMAN, XPS, Photoluminescence, and Dynamic Light Scattering has been analyzed. Squid measurement shows successful structural and magnetic property change in the shell region. Detailed synthesis, characterizations and application in nano-bio technology will be discussed.

206A. Synthesis of nano-bio hybridization of polypeptide and Co3O4 and characterize the composite material for device applications. <u>Bithi Paul</u>, Abdulla Al Mamun, Reaz Mahmud, Ahmed Rayhan Mahbub, and Kartik Ghosh. *Physics, Astronomy and Materials Science, Missouri State University, Springfield, MO* 65897.

Inorganic-bio nano-conjugates with cells, organelles, and intracellular structures containing DNA, RNA, and proteins establish sequences of nano-bio boundaries that depend on several intricate complex bio physicochemical reactions. Bio polypeptide nanostructures exhibit a unique type of self-assembled bio-materials having many interesting properties as well as applications. Piezoelectric activity is one of the interesting characteristic that has been found on inorganic- bio polypeptide nanotubes. In this work polypeptide nanotube was made using diphenyl, hexafluoride isopropanol (HFIP) and deionized water using sol-gel method. The peptide tubes were hybridized with inorganic materials Co3O4 through the reduction of Co ions from CoCl2 aqueous solution with the heat treatment. The composite of polypeptide and metal oxide nanomaterial (Co3O4) can be used as energy storage as well as electromagnetic applications. The formation of polypeptide/Co3O4 nano-bio composite has been probed using x-ray diffraction, Raman spectroscopy, scanning electron microscopy, and photo luminesce spectroscopy. Detailed results will be discussed in this presentation. Key words: Piezoelectricity, polypeptide nanotube, nano-bio hybrid.

206B. Block Copolymer Lithography. <u>Krishna Pandey</u>, C. Gunder, and M. Biswas. *Department of Physics, Astronomy & Materials Science, Missouri State University, Springfield, MO 65897.*

The inherent beauty of molecular self-assembly and potential of block copolymers (BCPs) nanopatterning in various applications received substantial attention in the field of nanotechnology [1]. The dissimilar blocks of BCPs can separate into distinct domains with periodic dimensions and functionalities in the nanometer scale through microphase separation. The typical dimension of the separated block domains is in the range of 5-100 nm, a dimensional span required for the future microelectronics and optoelectronics industry to thrive. The microphase separation depending upon molecular composition and chain architecture of BCPs leads to various structures, like spheres, cylinders, gyroid, lamellae [2]. The well-ordered periodic nanostructure of BCPs can be used for patterning inorganic oxide. In this presentation, we will present the nanofabrication of BCP nanostructures using cylindrical polystyrene-blockpoly (methyl methacrylate) (PS-b-PMMA) and micelles structures polystyrene-block-poly(2-vinylpyridine) (PS-b-P2VP) BCP. We will also present our ongoing work on

using these nanostructures as templates for the TiO2 deposition. The unique structural and functional properties of TiO2 have huge application in the area like photo catalysis, water splitting, solar cells, super capacitors and lithium-ion batteries [3]. We plan to deposit the TiO2 inside the selective blocks of block copolymers using two methods: solution deposition process and pulse laser deposition (PLD) method. After removing the polymer by calcination, the inorganic TiO2 pattern can be used in various microelectronic, optoelectronic and catalytic applications. References: 1. G. Krausch and R. Magerle, Advanced materials,14,21, (2002). 2. Y. Tseng et. al., Polymers, 2, 470-489, (2010). 3. M. Ge et. al., Journal of Materials Chemistry A, 4, 6772, (2016).

207A. Liquid Exfoliation of hexagonal Boron Nitride (h-BN) in various solvents. <u>Mohyammad Alneari</u> and Serif Uran. *Physics Department, Pittsburg State University, Pittsburg, KS* 66762.

Hexagonal boron nitride has attracted considerable attention due to its excellent electrical, mechanical and thermal properties. It has a layered structure similar to graphite and the layers are held together by Van der Waals forces. In our study, we tried to break the Van der Waals forces via various solvents and find the best solvent that exfoliates h-BN most efficiently and cleanly. The solvents use in our study are distilled water, Ammonia, and Acetonitrile. The samples were characterized via UV-Vis spectrometer and Optical microscopy. Various h-BN and solvent concentrations were studied and the results will be presented.

207B-U. Ultrasonic Characterization of Trabecular Bone Phantom Attenuation and Speed of Sound at 0.5 MHz. <u>Matthew Huber</u> and Brent Hoffmeister. *Physics Department, Rhodes College, Memphis, TN 38112.*

Ultrasound is being researched and used for diagnosing osteoporosis. Researchers use trabecular bone from humans as a test material, but such bone is biohazardous, not uniform, and of limited size. This study evaluates the acoustic properties of commercially available open-cell polyurethane foam, known as "Sawbones", to see if it could pose as a substitute for trabecular bone in ultrasound studies. Methods: Sawbones trabecular bone phantoms with densities of 5.5, 7.5, 15, and 30 pounds per cubic foot were cut in rectangular slices. Each slice was scanned using a 0.5 MHz transducer. Based on the power loss of the reflected signal and the time-of-flight, the normalized broadband ultrasonic attenuation (nBUA) and speed of sound through the phantom were found. Results: The speed of sound and attenuation in Sawbones were observed to be stable even after being soaked in water. Additionally, attenuation values exhibited anisotropy. Attenuation increased with density from a nBUA of 5.60

up to 27.4 dB/cm/MHz. Speed of sound also generally increased with density, ranging from 1550 to 1740 m/s. The accepted value for human bone trabecular bone nBUA at 0.5 MHz is 15.4 ± 25 dB/cm/MHz, and the speed of sound through bone is considered to be 2177 ± 701 m/s. Conclusions: The attenuation and speed of sound for different Sawbones densities were characterized at 0.5 MHz, a frequency commonly used in medical ultrasound, with results comparable to those expected in human bone. Furthermore, the material is stable in water, facilitating reliable measurements, and exhibits anisotropy, a characteristic of human bone. These findings provide a foundation for using Sawbones trabecular bone phantoms as an alternative to real trabecular bone in ultrasound studies. This work was supported by NIH grant R15AR066900.

208A-U. No Title Submitted. <u>Phoebe Sharp</u>, Joey McPherson, and Brent Hoffmeister. *Physics Department, Rhodes College, Memphis, TN 38112.*

Osteoporosis is a degenerative bone disease that affects 54 million people a year1. Ultrasonic techniques may be used to detect changes in bone caused by osteoporosis. As osteoporosis progresses, bone becomes less dense and less attenuating to ultrasound. Thus, techniques that are sensitive to attenuation may be useful for diagnostic purposes. The goal of this study was to measure a damping coefficient based on backscatter measurements of bone. Backscatter measurements were performed by propagating ultrasonic pulses into 29 cube shaped specimens of human bone and receiving the returned "backscattered" signal. The amplitude of the backscattered signal decreased exponentially as ebt, where b is defined to be the damping coefficient caused by attenuation. The damping coefficient b was found to increase with bone density. The damping constant demonstrated moderate to strong correlations with bone density (0.4 < R2 < 0.6). Thus, techniques based on the damping of backscatter signals by attenuation may be a useful way to detect changes in bone caused by osteoporosis.

208B-U. Evaluating Ultrasonic Backscatter Sensitivity to Microstructural Characteristics of Porous Bone. Joshua Moore, Brent Hoffmeister, Luke Fairbanks, and Sheldon Ebron. *Physics Department, Rhodes College, Memphis, TN 38112.*

Osteoporosis is a bone disease characterized by decreased bone density and structural deterioration of bone tissue. This study evaluates the sensitivity of ultrasonic measurements to microstructural characteristics of bone determined by x-ray micro CT analysis. Fifty-five cube-shaped specimens of bone were prepared from 14 cadaveric femurs. Micro CT measurements were performed to obtain 7 microstructural parameters (BV/TV, Conn.Dens., TRI- SMI, Tb.N, Tb.Th, Th.Sp, App.BMD) for each specimen. In addition, ultrasonic backscatter measurements were performed on each specimen using a 3.5 MHz transducer. The ultrasonic signals were analyzed to determine 4 backscatter parameters (nMBD, nSBD, nIBD, nBAR). Linear regression analysis was used to determine the degree of correlation between the ultrasonic and micro CT parameters. Strongest correlations were observed between nMBD and App.BMD, (0.76 < |R| < 0.93). The weakest correlations were observed between the parameters nIBD and Conn.Dens. (0.02 < |R| < 0.28). It appears that the ultrasonic parameters correlate with certain micro CT parameters, namely nMBD and App.BMD.

209A-U. Techniques to Optimize Endothelial Cells Attachment to Microcarrier Beads and Recovery, Achieving the State of Weightlessness Following Radiation. <u>Calla Bassett</u>, Abdel Bachri, Rupak Pathak, Sanchita P. Ghosh, Igor Koturbash, Marjan Boerma, Regina K. Binz, Jeffrey R. Sawyer, and Martin Hauer-Jensen. *Engineering and Physics, Southern Arkansas University, Magnolia, AR* 71753.

In order to study whether the exposure to space radiation and near zero gravity contribute to an increased risk for cardiovascular disease, we irradiate Human Umbilical Vein Endothelial Cells (HUVECs), and subject them to ground-based simulated microgravity. HUVECs are used because cardiovascular diseases have been linked to genomic instability in endothelial cells. We use the High Aspect Ratio Vessel (HARV) bioreactor to seed the cells onto Cytodex-3 microcarrier beads and cause them to undergo free suspension, a condition similar to near zero gravity in the outer space. A key component for this experiment is to standardize the microcarrier bead concentration, cells attachment and the HARV rotation speed to achieve free suspension. This standardization is required in order to prevent damage to the cells during the long microgravity treatment and optimize cell recovery. We discuss standardization techniques to improve cell attachment and microgravity treatment. Next we characterize chromosome aberrations of irradiated HUVECs with Fluorescence in Situ Hybridization (FISH) and Spectral Karyotyping (SKY). We found that vitamin E ytocotrienol (GT3) pretreatment reduced double strand break formation in HUVECS, and decreased chromosome aberration in HUVECs and mouse bone marrow cells after irradiation. Work is currently undergoing to address how space radiation interact with microgravity to find their combined effect on chromosome aberrations.

209B-U. Modifying Snipe It to organize inventory. Zaire Husband and Tom Coffin. Computer Science Department, University of Arkansas at Little Rock, Little Rock, AR 72204. My project was to set up and program "Snipe It" for easy access to UALR's Emerging Analytical Center's (EAC) inventory. Snipe It is an open source inventory management system. Snipe It operates on the web primarily through the script language Hyper Preprocessor (PHP) and Structured Query Language (SQL). I originally tried to create the program environment on a windows system, but found it difficult. Although, I could write files more easily in Windows, I found an alternative system called Ubuntu that allowed me to send direct commands from the terminal into Snipe It. Even though Snipe It already has working functions, I set up and created the platform for Snipe It to work from. Snipe It only worked with specific environments that supported both PHP and SQL. At first, the system did not allow for any kind of manipulation aside from the default database created, however, I later on deduced that this was due to the MySQL, software that works with SQL, having an automatic security key that needed to be reprogrammed. I had to enter MySQL's basic coding and rewrite the access key to change the databases. I also had to find and implement PHP extensions for Snipe It to run its full features. Once I got the pre-flight and setup working properly, I input all of the EAC's assets into the system. This required adding appropriate information such as license, purchase date, location and categories to over 50 assets in the system. After my initial setup in the terminal, the user interface was very simple to use and easy understand. Since Snipe It is an open source software, any user with a bit of knowledge about PHP and SQL can add and improve the system for better management and faster service.

210A-U. Lysenin-Dipole Strength Controls its Gating.

Radwan Al Faouri, Jess Ray, <u>Chidubem Egbosimba</u>, Ralph Henry, and Greg Salamo. *Physics Department, University of Arkansas, Fayetteville, AR* 72701.

Lysenin is a 297 amino acid pore-forming toxin that is isolated from the coelomic fluid of the earthworm Eisenia foetida. It is a self-inserted protein that form large conductance pores (~3nm) into bilayer lipid membranes containing sphingomyelin (Fig. a). Lysenin channels exhibit voltage induced gating and activity modulation by ionic strength and pH, suggesting that electrostatic interactions play a major role in establishing their electrical activity. Electrostatic surface representation of the lysenin (Fig. b) reveals a distribution of fixed positive charges (blue) on the Cterminal and negative fixed charges (Red) on the Nterminal (inside the lumen of the channel) proposing a dipole moment along the structure of this protein. In this line of inquiries, we suggest that the movement of the C-terminus of Lysenin causes its voltage induced gating. Accordingly, the modification of the strength of the dipole moment that interacts with the applied

external electric field influences voltage induced gating of the lysenin. The negative charges in the N-terminal is reduced by replacing the two glutamates in the wild type lysenin (Fig. c) with two alanine amino acids and our results show that higher electric field is required to start the voltage gating of the modified lysenin. On the other hand, we inspected the ligand induced gating of lysenin by investigating the interaction of different multivalent ions with lysenin channels at specific monovalent ion concentration (electrolyte solution). We hypothesize that monovalent and multivalent cations compete for a binding site (negative charges on the Nterminal) of lysenin. In particular, we inspected the interaction of iron divalent cations with the binding site of lysenin for both wild type and modified lysenin. Our results show inhibition of the macroscopic conductance of a population of lysenin channels in a concentration dependent manner of iron divalent cations. The higher sensitivity encountered towards low monovalent ions concentration supports our assumption of a competition between monovalent and iron divalent cations on the binding site of lysenin. Understanding the mechanism of gating of this protein will have a direct impact on drug delivery applications when using these pores (lysenin channels) in liposomes as drug carriers.

210B. Robust non-parametric descriptors for the quantification of clustering features of molecules in single-molecule localization microscopy. <u>Shenghang Jiang</u>, Sai Divya Challappalli, and Yong Wang. *Physics Department, University of Arkansas, Fayetteville, AR* 72701.

Recent developments of single-molecule localization microscopy (SMLM) have enabled more quantitative analyses on spatial organizations of biological molecules inside live cells, providing new and crucial information that was not accessible before. Here, we report a robust non-parametric descriptor for quantifying the spatial organization of molecules from SMLM data. We discovered that the derivative of a J-function that is based on nearest neighbor distances, J'(r), provides valuable information about the spatial patterns of molecules. We determined the relationship between various characteristics of clustering points and the J'(r) descriptor, and found that it can reliably quantify the characteristics of these clustering point patterns without any human entered parameters. More specifically, the position of the derivative function J'(r), rJ'm, relies only on the density of clustering points (pc). We also demonstrated that this rJ'm-pc relation is robust in the presence of high noise levels. As a result, our descriptor is ideal for direct measurements of clustering density of molecules in single-molecule localization microscopy.

211A. Tuning Optoelectronic Properties of Single-Walled Carbon Nanotubes by Selective Adsorption of Sodium Dodecyl Sulfate (SDS). Jakob Hockman, Arvind Sinha, and Jin-Woo Kim. Cell and Molecular Biology, University of Arkansas, Fayetteville, AR 72701.

Gel filtration with sodium dodecyl sulfate (SDS) dispersed single-walled carbon nanotubes (SWNTs) was used to separate SWNTs based on electronic and optical subtypes. Samples enriched in either metallic or semiconducting SWNTs (m- and s-SWNTs, respectively) were isolated and characterized using absorbance spectroscopy using a method optimized for biological applications. At least three unique peaks in the nearinfrared region were detected from separated samples in semiconducting SWNTs. The optical response of individual nanotube samples was shown to be dependent on the length of sonication used to disperse the SWNTs. We successfully demonstrated the use of this method to tune the optical and electronic properties of SWNT-based materials for biological applications.

211B. Effects of High Hydrostatic Pressure on the budding of Saccharomyces cerecisiae. <u>Khanh Nguyen</u>, Steven Murray, Jeffrey Lewis, and Pradeep Kumar. *Physics Department, University of Arkansas, Fayetteville*, *AR 72701.*

Saccharomyces cerevisiae or budding yeast is a common yeast used in baking bread, brewing, and wine making through a process called alcoholic fermentation. S.cerevisiae is used as a model for more complex eukaryotic cells due to its simplicity and wide array of knowledge on the organism. Yeast cells reproduce through a division process called budding. To investigate how pressure affects the budding process of yeast, we investigated the budding index of S. cerevisiae in a wide range of pressures (1-500 atm). After the exposure to high pressure, the images of the cells were taken using a microscope and the budding index of the cells were quantified using a home-brewed program. We find that the budding yeast exposed to higher pressures has a lower budding index compare to the one at normal pressure, suggesting the high hydrostatic pressure suppresses the budding of cells.

212A-U. Adhesive Force between Graphene Nanoscale Flakes and Biological Cells. Radwan Al Faouri, <u>Christopher Oldfield</u>, Ralph Henry, and Greg Salamo. *Biomedical Engineering, University of Arkansas, Fayetteville, AR* 72701.

We report on a measurement technique that quantifies the adhesive force between graphene flakes and the cell wall of live E.coli cells using atomic force microscopy (AFM) in fluid Peak Force QNM mode. To measure the adhesive force we made use of the negative charge of E.coli cells to allow them to stick to positively charged surfaces such as glass or silicon that were covered with polylysine. For example, with this approach the cells were held in place during the AFM measurements. In this way, AFM was used to characterize the size of graphene flakes, both functionalized and nonfunctionalized, on E.coli cells that were held on a silicon substrate. We correlated these measurements with AFM measurements of the adhesive force between graphene and the cell wall of E.coli cell. Using this approach, the measured values of the adhesive force between graphene and E.coli was determined to be greater than 450(+/- 40) pN for the non-functionalized graphene.

212B-U. The Uses of Instrumentation to Study Material Characteristics. <u>Octie Ashley</u>, Joidan Romes, Wei Du, Mansour Mortazavi. *Physics Department, UA Pine Bluff, Pine Bluff, AR* 71601.

Throughout a 10-week research internship with the Department of Chemistry and Physics at the University of Arkansas at Pine Bluff different instrumentation methods were used to study material characteristics. The Scanning Electron Microscope, the Photoluminescence Spectroscopy, and the Raman Spectroscopy were used to research given samples.

213A. Temperature dependence of the multistability of the lactose utilization network of Escherichia coli. <u>Sudip Nepal, Kionna Henderson</u>, Sara Diletti, Pradeep Kumar. *Micro-Ep, University of Arkansas, Fayetteville, AR 72701.*

Biological systems are capable of producing multiple states out of a single set of inputs [1]. Multistability acts like a biological switch that allows organisms to respond differently to different environmental conditions and hence plays an important role in adaptation to changing environment. One of the widely studied gene regulatory networks underlying the metabolism of bacteria is the lactose utilization network [2,3], which exhibits a multistable behavior as a function of lactose concentration. Here we study the effect of temperature on multistability of the lactose utilization network at various concentrations of thio-methylgalactoside (TMG), a synthetic lactose. We find that while the lactose utilization network exhibits a bistable behavior at high temperature, a graded response arises for temperature T<20C. Further, we construct a phase diagram of the graded and bistatble response as a function of temperature and TMG concentration. References: M. Ptashne, "A Genetic Switch: Gene control and Phage Lambda.", Cold Spring Harbor Laboratory Press New York, 3rd Edition (2004). F. Jacob and J. Monod, "Genetic regulatory mechanisms in the synthesis of proteins.", Journal of Molecular Biology 3, 318-356

(1961). E. M. Ozbudak et. al., "Multistability in the lactose utilization network of Escherichia coli." Nature 427, 737-740 (2004).

213B-U. Structural characteristics of Au-GaAs nanostructures for increased plasmonic optical enhancement. <u>Zachary T. Brawley</u>¹, Stephen J. Bauman², Grant P. Abbey², Ahmad A. Darweesh², Ahmad I. Nusir², Omar Manasreh², and Joseph B. Herzog². ¹Physics Department, University of Central Arkansas, Conway, AR 72035 and ²Physics Department, University of Arkansas, Fayetteville, AR 72701.

This research explores how various geometries and characteristics of Au plasmonic nanostructures on the plane of a GaAs semiconductor improve the total optical enhancement in the GaAs photodetectors. Computational models were built to study these characteristics. Varying the electrode spacing, Au width, and Au thickness were shown to drastically affect the amount of enhancement in the GaAs. Peaks in enhancement were observed at specific Au widths and thicknesses resonant with the incident wavelength of 875 nm. The intensity of these peaks decayed as the widths and thicknesses increased. In addition, a simulation was run with a Ti adhesion layer between the Au and the GaAs. It was shown that as the Ti thickness increased, the optical enhancement in the GaAs decreased. Optimal dimensions for the photodetector were then found.

214A-U. Effect of Hind-Limb Suspension and X-Ray Irradiation on Elasticity of Rat Femur and Tibia Bone. Hayley Heacox, B. Hill, R. Mehta, J.S. Barajas, L.M. Benzmiller, S.G. Freyaldenhoven, M. Dobretsov, and P. Chowdhury. *Physics Department, University of Central Arkansas, Conway, AR* 72035.

It is known that space conditions such as microgravity and cosmic radiation have detrimental effects on the skeletal system of humans, such as decreased bone mineral density. This research aims to study the changes in elasticity of rat femur and tibia bones when exposed to space-like conditions of simulated microgravity and cosmic radiation. It is hypothesized that if microgravity and cosmic radiation lead to decreased bone mineral density, then these conditions will produce weakened bones as compared to bones not subject to these conditions. Three different experiments were performed to investigate these elastic alterations. In experiment 1, a group of rats was exposed to a 2.0 GY xray radiation dose that was administered over a 3-4-day interval period (IR) while a separate group served as controls (CON). In experiments 2 and 3, a group of rats was subject to hind limb suspension (HLS) for approximately two weeks in order to imitate microgravity. A second group was exposed to the same radiation protocol as described above (IR). A third group of rats was exposed to both variants- two weeks of hind limb suspension and a 2.0 GY dose of x-ray radiation (HLS-IR). Finally, a control group consisted of nonirradiated and non-suspended rats (CON). A technique known as three-point bending was employed in which a known amount of force is exerted upward perpendicular to the middle of each bone (tibia and femur), which is held fixed at each end by a specially developed holder. A motorized force transducer performed the upward force. Using two software programs, the force applied at each distance is recorded in real time. A modified Euler-Bernoulli beam theory equation was applied to estimate the Young's (elastic) modulus for the leg bones. A lessening of the elastic modulus is indicative of weakening of the bone. Analysis of results suggest a less elastic nature of leg bones exposed to HLS or IR compared to leg bones that were not suspended or irradiated; this weakening wass more apparent in the tibias. When the effects of HLS and IR are combined, a weakening of the bones was observed but not in as great of magnitude as hypothesized. + This work supported by a RID and CRP grant from Arkansas Space Grant Consortium.

214B-U. Neutron Capture Elements in Low Metallicity Stars within the Galactic Halo. <u>Kenneth A. Jumper</u> and Debra L. Burris. *Physics and Astronomy, University of Central Arkansas, Conway, AR* 72035.

The inner galactic halo is home to some of the oldest and low metallicity stars known. These stars are local enough to observe heavy element synthesis in the oldest stars in our galaxy. The purpose of this research is to analyze the distributions of neutron capture elements in low metallicity stars to help us understand the nature of first stars, which are responsible for the chemical enrichment of our galaxy, and consequently get man closer to an answer to some of the most fundamental questions about the universe. This project will analyze and measure the stellar abundances of metal poor stars using the spectral synthesis program MOOG. Heavy element formation is connected to stellar evolution, thus by observing the chronometric ages of the distributions of Thorium/Europium, one can determine the age of the oldest stars. Analyzing the distribution of Uranium and Thorium as chronometers can set a lower limit on the age of the Universe. The chemical composition in the oldest observable stars resemble that of the earliest stars. This demonstrates that these elements were not synthesized internally but a result of previous deaths of stars generations before. This provides useful information about the first star's formation, evolution and nucleosynthesis of stars, and the arrangement of the structure of the early Universe. The most r-process rich halo stars abundances are consistent with a scaled solar system r-process abundance distribution. However, the lighter n-capture abundances don't conform to the solar pattern. This

suggests the possibility of multiple synthesis mechanisms for the n-capture elements. The combinations could include the main r-process, V-P process (core collapsed super-novae), charged particle reactions with Beta delayed fission, and the weak rprocess.

215A-U. Mass Determinations of AGNs using Spectroscopy. <u>T. Jacob Cameron</u> and Debra L. Burris. *Physics and Astronomy, University of Central Arkansas, Conway, AR* 72035.

At the center of some active galaxies are super-massive black holes and for some time the accepted method of measuring the mass of such galaxies has been the method used by Vestergaard and Peterson, among others. By using the luminosity function which is related to H- β emission spectra from these black holes, both for cosmic redshift and for Fe-II emissions using IRAF. From there, H- β can accurately measure the full width half max of the H-beta line in these spectrum as well as the luminosity and these paired with the O-III lines give us an estimate on the mass of the black hole. The purpose of this is to compare it to the values obtained from the Mass-Pitch Angle relation being proposed by Kennefick et al. (2016 in preparation)

215B. Structural and dielectric properties of O.5Ba(Zr0.2Ti0.8)O3-0.5(Ba0.7Ca0.3)TiO3/LSMO/LAO lead free epitaxial ferromagnetic thin films by Pulsed Laser Deposition(PLD). <u>Md Abdullah-Al Mamun</u>, Anthony Pelton, Bithi Paul, and Kartik Ghosh. *Physics, Astronomy & Materials Science, Missouri State* University, Springfield, MO 65897.

Lead free epitaxial thin films were prepared to replace the popular Pb-based ferroelectric, PZT. We deposited BZT-BCT on La0.7Sr0.3MnO3(LSMO) by laser ablation. Prior to that, LSMO was deposited on Lanthanum Aluminate (LAO) applying the same ablation procedure. We maintained the morphotropic phase boundary conditions (that is 0.5-0.5 for BZT-BCT ceramic) for the enhancement of dielectric, piezoelectric and electromechanical properties. X-ray diffraction of the hetero-structure represents high degree of tetragonality, which might be the cause for enhanced dielectric properties. Vibrational mode was characterized through Raman Spectroscopy. We measured the field-cooled and zero field-cooled magnetization at room temperature through Superconducting Quantum Interference Device (SQUID). The Ferro-Magnetic Resonance (FMR) of the film was measured. Also, the dielectric properties of the films were measured. The analysis of all those data concluded that PLD grown hetero-structure might be a solution to replace toxic Pb-based materials. The inclusion of LSMO between BZT-BCT and LAO was an invention that might open up a new thinking of research.

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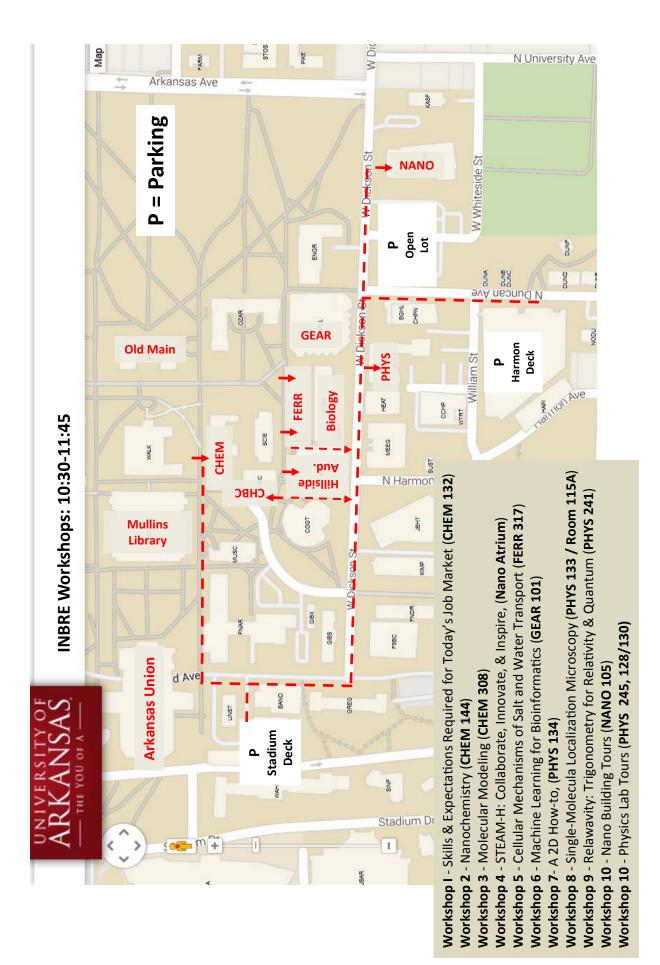
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