STATE OF ARKANSAS
MIKE BEEBE
GOVERNOR

November 15, 2013

It gives me great pleasure to send greetings to all those gathered in Little Rock for the 2013 Southeast Regional IDeA Meeting, hosted by the Arkansas IDeA Network of Biomedical Research Excellence (INBRE) and the Centers of Biomedical Research Excellence (COBRE). Welcome to our visitors from Arkansas, Louisiana, Mississippi, Puerto Rico, South Carolina, West Virginia, and Kentucky. We are delighted to have you in our State, and I know that the residents of our capital city will do everything possible to make your stay here a pleasant and memorable experience.

IDeA, or the Institute Development Award, is designed to broaden the geographic distribution of funding from the National Institutes of Health (NIH) for biomedical research. As authorized by Congress, the program works to enhance the competitiveness for research funding of institutions located in states with historically low levels of funding and low aggregate success rates for grant applications to the NIH. This year’s conference will offer presentations by officials from the NIH, speakers in various fields of biomedical research, and IDeA faculty, postdoctoral fellows, and students. Their focus will be bioinformatics, cancer, cardiovascular research, cell signaling, infectious disease/immunology, and neuroscience.

Arkansas has benefitted greatly from grants made by the National Institute of General Medical Sciences at the NIH through the Institutional Development Award (IDeA) program. The INBRE award has established a statewide network that links Arkansas institutions of higher education, while the COBRE program has created a number of successful multidisciplinary research centers around the State. These programs have expanded and developed our research infrastructure and helped build the biomedical research capacity in Arkansas, for which we are grateful.

I am confident each of you will enjoy everything Arkansas has to offer: warm hospitality, excellent accommodations, fine dining, and a wealth of entertainment. On behalf of the State of Arkansas, best wishes for a productive and stimulating meeting.

Sincerely,

Mike Beebe

MB:jb
# Table of Contents

**Meeting Committees**
- Steering Committee ........................................................................................................ 3
- Logistics Committee ........................................................................................................... 3
- Scientific Review Committee .......................................................................................... 3

**Meeting Agenda** .................................................................................................................. 4

**Meeting Floor Plan** ............................................................................................................. 5

**Welcome Reception at the William J. Clinton Presidential Center** ........................................... 6

**Breakfast Topic Tables** .......................................................................................................... 7

**Student Lunch Panel** ........................................................................................................... 7

**Speaker Biographies**
- Plenary Speakers .............................................................................................................. 10
- Invited Speakers .................................................................................................................. 12

**Scientific Sessions, Saturday, November 16** ..................................................................... 16

**Scientific Sessions, Sunday, November 17** ...................................................................... 20

**Scientific Session Abstracts**
- Bioinformatics I ................................................................................................................ 24
- Cancer I ............................................................................................................................... 26
- Cardiovascular Research .................................................................................................. 29
- Cell Signalling ................................................................................................................... 31
- General Biomedical Sciences ............................................................................................ 34
- Infectious Disease/Immunology I ..................................................................................... 36
- Neuroscience .................................................................................................................... 39
- Undergraduate Research ................................................................................................. 41
- Bioinformatics II .............................................................................................................. 44
- Cancer II ............................................................................................................................ 47
- Infectious Disease/Immunology II ..................................................................................... 49

**Poster Session Abstracts**
- Bioinformatics ................................................................................................................ 54
- Cancer ................................................................................................................................. 63
- Cardiovascular Research .................................................................................................. 79
- Cell Signalling ................................................................................................................... 83
- General Biomedical Sciences ............................................................................................ 91
- Infectious Disease/Immunology ....................................................................................... 111
- Neuroscience .................................................................................................................... 118

**Sponsor Acknowledgements** ............................................................................................ 146

**Meeting Attendees** ............................................................................................................ 147

**Index**
- Abstracts by Thematic Areas ............................................................................................ 156
- Abstracts by Presenter ........................................................................................................ 164
<table>
<thead>
<tr>
<th>Steering Committee</th>
<th>Logistics Committee</th>
<th>Scientific Review Committee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lawrence E. Cornett, Ph.D. (Chair)</td>
<td>Alan Tackett, Ph.D. (Chair)</td>
<td>Helen Beneš, Ph.D. (Co-Chair)</td>
</tr>
<tr>
<td>University of Arkansas for Medical Sciences</td>
<td>University of Arkansas for Medical Sciences</td>
<td>University of Arkansas for Medical Sciences</td>
</tr>
<tr>
<td><a href="mailto:LCornett@uams.edu">LCornett@uams.edu</a></td>
<td>Alan Tackett, Ph.D.</td>
<td>Prakash Nagarkatti, Ph.D.</td>
</tr>
<tr>
<td>Helen Beneš, Ph.D.</td>
<td>University of Arkansas for Medical Sciences</td>
<td>University of South Carolina</td>
</tr>
<tr>
<td>University of Arkansas for Medical Sciences</td>
<td>University of Arkansas for Medical Sciences</td>
<td><a href="mailto:PRAKASH@mailbox.sc.edu">PRAKASH@mailbox.sc.edu</a></td>
</tr>
<tr>
<td><a href="mailto:BenesHelen@uams.edu">BenesHelen@uams.edu</a></td>
<td>Caroline Miller Robinson</td>
<td>Eric C. Rouchka, Ph.D.</td>
</tr>
<tr>
<td>Edgar Garcia-Rill, Ph.D.</td>
<td>University of Arkansas for Medical Sciences</td>
<td>University of Louisville</td>
</tr>
<tr>
<td>University of Arkansas for Medical Sciences</td>
<td>Caroline Miller Robinson</td>
<td><a href="mailto:ecrouc01@louisville.edu">ecrouc01@louisville.edu</a></td>
</tr>
<tr>
<td><a href="mailto:garciarilledgar@uams.edu">garciarilledgar@uams.edu</a></td>
<td></td>
<td>Glen Shearer, Ph.D.</td>
</tr>
<tr>
<td>Roger E. Koepp, II, Ph.D.</td>
<td></td>
<td>The University of Southern Mississippi</td>
</tr>
<tr>
<td>University of Arkansas</td>
<td></td>
<td><a href="mailto:glen.shearer@usm.edu">glen.shearer@usm.edu</a></td>
</tr>
<tr>
<td><a href="mailto:rk2@uark.edu">rk2@uark.edu</a></td>
<td></td>
<td>Scott R. Whittemore, Ph.D.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>University of Louisville School of Medicine</td>
</tr>
<tr>
<td></td>
<td></td>
<td><a href="mailto:swhttemore@louisville.edu">swhttemore@louisville.edu</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rhonda L. Anthony</td>
</tr>
<tr>
<td></td>
<td></td>
<td>University of Arkansas for Medical Sciences</td>
</tr>
<tr>
<td></td>
<td></td>
<td><a href="mailto:RLANAnthony@uams.edu">RLANAnthony@uams.edu</a></td>
</tr>
</tbody>
</table>
### Friday, November 15, 2013

<table>
<thead>
<tr>
<th>Time</th>
<th>Location</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>3:00 – 6:00 PM</td>
<td>Balcony</td>
<td>Registration, Little Rock Marriott</td>
</tr>
<tr>
<td>5:30 – 9:00 PM</td>
<td>Great Hall</td>
<td>Welcome Reception at the William J. Clinton Presidential Center</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Transportation provided.</td>
</tr>
</tbody>
</table>

### Saturday, November 16, 2013

<table>
<thead>
<tr>
<th>Time</th>
<th>Location</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:30 AM</td>
<td>Salons B &amp; C</td>
<td>Registration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Breakfast Table Topics &amp; Networking</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poster Set-up</td>
</tr>
<tr>
<td>8:15 AM</td>
<td>Salon A</td>
<td>Judges’ Meeting</td>
</tr>
<tr>
<td>8:30 AM</td>
<td>Salon A</td>
<td>Welcome and Opening Remarks – Lawrence Cornett, Ph.D., Director AR INBRE</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Speaker Introduction - Fred Taylor, NIGMS, Chief of Capacity Building Branch</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Plenary Speaker - Jon R. Lorsch, Ph.D., NIGMS Director</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Régine Douthard, M.D., M.P.H., Medical Officer, NIGMS IDeA Program</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Jim Hoehn, EPSCoR Coalition, EPSCoR/IDeA Foundation Update</td>
</tr>
<tr>
<td>10:00 - 10:30 AM</td>
<td>Balcony</td>
<td>Break – light refreshments</td>
</tr>
<tr>
<td>10:30 - 12:00 PM</td>
<td>Breakout Rooms</td>
<td>Concurrent Sessions 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Session 1A – Bioinformatics I (Manning)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Session 1B – Cancer I (Salon A)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Session 1C – Cardiovascular Research (Arkansas Ballroom)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Session 1D – Cell Signalling (Hoffman)</td>
</tr>
<tr>
<td>12:00 PM</td>
<td>Salons B &amp; C</td>
<td>Lunch Networking &amp; Vendor Exhibit &amp; Poster Viewing</td>
</tr>
<tr>
<td>1:30 – 2:30 PM</td>
<td>Salon A</td>
<td>Plenary Speaker - Carole Cramer, Ph.D.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Plant-made Pharmaceuticals – “Delivering” Enzyme Therapeutics for Rare Diseases</td>
</tr>
<tr>
<td>2:30 – 2:45 PM</td>
<td>Balcony</td>
<td>Break – light refreshments</td>
</tr>
<tr>
<td>2:45 – 4:15 PM</td>
<td>Breakout Rooms</td>
<td>Concurrent Sessions 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Session 2A – General Biomedical Sciences (Hoffman)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Session 2B – Infectious Disease/Immunology I (Manning)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Session 2C – Neuroscience (Salon A)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Session 2D – Undergraduate Presentations (Arkansas Ballroom)</td>
</tr>
<tr>
<td>3:00 PM</td>
<td>Salons B &amp; C</td>
<td>Graduate School Exposition</td>
</tr>
<tr>
<td>4:30 PM</td>
<td>Salons B &amp; C</td>
<td>Poster Session &amp; Reception</td>
</tr>
<tr>
<td>6:30 PM</td>
<td></td>
<td>Dinner on your own</td>
</tr>
</tbody>
</table>

### Sunday, November 17, 2013

<table>
<thead>
<tr>
<th>Time</th>
<th>Location</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:30 AM</td>
<td>Balcony</td>
<td>Breakfast Table Topics &amp; Networking</td>
</tr>
<tr>
<td>8:30 - 9:30 AM</td>
<td>Salon A</td>
<td>Commercialization of Biomedical Research – Panel Discussion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Speaker Introduction – Helen Beneš, Ph.D., Coordinator AR INBRE</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Invited Speaker: Robert Vinson, NIH SBIR/STTR, Overview of the NIH SBIR/STTR Program</td>
</tr>
<tr>
<td>9:30 AM</td>
<td>Balcony</td>
<td>Break – light refreshments</td>
</tr>
<tr>
<td>10:00 - 11:30 AM</td>
<td>Breakout Rooms</td>
<td>Concurrent Sessions 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Session 3A – Bioinformatics II (Hoffman)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Session 3B – Cancer II (Salon A)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Session 3C – Infectious Disease/Immunology II (Manning)</td>
</tr>
<tr>
<td>11:30 AM</td>
<td>Salon A</td>
<td>Student Award Announcements</td>
</tr>
</tbody>
</table>
Meeting Floor Plan

MEETING ROOMS/BALLROOM LEVEL
Welcome Reception
William J. Clinton Presidential Center

Trolleys will be available from 5:30 PM until 9:00 PM in front of the Little Rock Marriott to shuttle Meeting attendees to and from the William J. Clinton Presidential Center.

Governor Mike Beebe will address the attendees at 6:00 PM in the Great Hall, which will be followed by a showing of Dr. Edgar Garcia-Rill’s documentary film, "Brain Power", a 7-minute film outlining the establishment of the University of Arkansas for Medical Sciences Center for Translational Neuroscience through a COBRE grant. Refreshments will be provided. The River Market District offers a wide variety of dining options. Please see the list of Staff Favorites in your packet for a list of area restaurants.

During the reception, the Clinton Presidential Library and Museum will be open to Meeting attendees for self-guided tours. It is located within the Clinton Presidential Center and Park in the River Market District of Little Rock. The Center includes the Clinton Foundation (Little Rock office) and the University Of Arkansas Clinton School Of Public Service.

In addition to the archival collection and research facilities, the Clinton Presidential Library and Museum features exhibits, special events, and educational programs. The museum includes replicas of the Oval Office and the Cabinet Room. Permanent exhibits utilize documents, photographs, videos and interactive stations. A timeline and alcoves highlight domestic and foreign policy, as well as life in the White House.

The American Presidency is part of a unique heritage that can be explored through archives, museums, and special programs, Presidential Libraries preserve the documents and artifacts of our Presidents and provide insight into the times in which these Presidents lived and served the nation.

The temporary exhibits at the museum are:

And Freedom for All: The March on Washington for Jobs and Freedom
August 10, 2013 – November 17, 2013

This exhibit pays tribute to the 50th anniversary of The March on Washington. The March took place in Washington, D.C., on August 28, 1963. It was attended by approximately 250,000 people, it was the largest demonstration ever seen in the nation's capital. Stanley Tretick was assigned by LOOK magazine to cover the march “behind-the-scenes” with organizers and program speakers. The exhibit features his pictures and videos of speeches by Daisy Bates, John Lewis and a performance by Mahaila Jackson.

Dr. Martin Luther King Jr’s “I Have a Dream” speech is featured in the exhibit. President Clinton declared the speech to be “the clearest clarion call to the more perfect union of America in the 21 century.”

Oscar de la Renta, American Icon
Exhibit Dates: May 18 - December 1, 2013

This seminal fashion exhibition celebrates the world-renowned work and inspiring life of designer Oscar de la Renta. The exhibit will feature more than thirty of his iconic creations worn by leading arbiters of style, from First Ladies to Hollywood’s brightest stars.

In the 1960s, Dominican-born Oscar de la Renta moved to the United States, where he launched his signature ready-to-wear label and quickly became known as a leading figure in international fashion design. Oscar de la Renta’s award-winning career spans five decades and he continues to produce an exceptional body of work – a testament to his enduring creative vision.
Breakfast Table Topics (EACH MORNING)

Breakfast Table Topics (BTTs) will be presented on both Saturday and Sunday from 7:30 AM until 8:15 AM. BTTs are intended to be an informal gathering with group discussion/interaction. Each table has an assigned topic and an expert in the field. We encourage you to join a table of your choice each morning and to bring your questions.

Saturday, November 16, 2013

<table>
<thead>
<tr>
<th>Topic</th>
<th>Expert</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>Minolfa C. Prieto, M.D., Ph.D., Assistant Professor</td>
</tr>
<tr>
<td>HPV-Mediated Cancer</td>
<td>Lucia A. Pirisi-Creek, M.D., Professor &amp; SC INBRE Program Director</td>
</tr>
<tr>
<td>Drug Design and Discovery</td>
<td>Seetharama Satyanarayanajois, Ph.D., Associate Professor</td>
</tr>
<tr>
<td>Proteomics</td>
<td>Roger Koenne, Ph.D., Professor &amp; AR INBRE Core Director</td>
</tr>
<tr>
<td>Core Management</td>
<td>Karen Martin, Ph.D., Director, WVU Imaging Facility</td>
</tr>
<tr>
<td>Neuroscience and Behavior</td>
<td>Craig A. Stockmeier, Ph.D., Professor &amp; Director Center for Psychiatric Neuroscience</td>
</tr>
<tr>
<td>Cancer Bioinformatics</td>
<td>Donald J. Johann, Jr., M.S., M.D., Associate Professor of Medicine &amp; Bioinformatics</td>
</tr>
<tr>
<td>Infectious Diseases</td>
<td>Antonieta Guerrero-Plata, Ph.D., Assistant Professor, School of Veterinary Medicine</td>
</tr>
</tbody>
</table>

Sunday, November 17, 2013

<table>
<thead>
<tr>
<th>Topic</th>
<th>Expert</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular and Kidney Function’</td>
<td>Daniel Kapusta, Ph.D., Professor and Director, COBRE CV Program</td>
</tr>
<tr>
<td>Proteomics</td>
<td>Julie Stenken, Ph.D., Professor, 21st Century Chair in Proteomics</td>
</tr>
<tr>
<td>Cellular &amp; Molecular Neuroscience</td>
<td>Rick Murray, Ph.D., Associate Professor &amp; AR INBRE Project Leader</td>
</tr>
<tr>
<td>Infectious Disease</td>
<td>Karl Boehme, Ph.D., Assistant Professor, Microbiology &amp; Immunology</td>
</tr>
<tr>
<td>Neuroscience and Behavior</td>
<td>Craig A. Stockmeier, Ph.D., Professor &amp; Director Center for Psychiatric Neuroscience</td>
</tr>
<tr>
<td>Protein Structure and Function</td>
<td>Frank Millett, Ph.D., Professor &amp; COBRE Director</td>
</tr>
<tr>
<td>Chemoinformatics</td>
<td>Robert J. Doerksen, Ph.D., Associate Professor, Medicinal Chemistry</td>
</tr>
<tr>
<td>Immunology</td>
<td>Sanjay Batra, Ph.D., Assistant Professor, Pathobiological Sciences</td>
</tr>
</tbody>
</table>

Student Career Luncheon (SATURDAY)

The Student Career Luncheon is designed to give students a glimpse of career opportunities in the sciences. A panel of five former INBRE funded students will give a brief overview of their career paths and answer questions about the opportunities and challenges of pursuing a scientific career.

Drew Jones: attended Hendrix College; graduated from the University of Arkansas for Medical Sciences with a Ph.D. in Biochemistry, and is currently doing a Post-Doctoral Fellowship at St. Jude Children’s Research Hospital in Memphis, Tennessee

Kirt Durand: attended University of Arkansas at Pine Bluff; currently in a Ph.D. Program at Purdue University in Indiana in Analytical Chemistry

Cody Cook: attended University of Central Arkansas; graduated from the University of Arkansas for Medical Sciences M.D./Ph.D. Program in Biochemistry and Molecular Biology

Joseph Levy: attended Ouachita Baptist University; currently in a M.D./Ph.D. Program at University of Arkansas for Medical Sciences in Radiation Oncology

Stephanie Byrum: attended Ouachita Baptist University; graduated with a Ph.D. from the joint UALR/UAMS Bioinformatics Program; currently a Post-Doctoral Fellow at the University of Arkansas for Medical Sciences
Speaker Biographies
Jon R. Lorsch, Ph.D., became the director of the National Institute of General Medical Sciences in August 2013.

As NIGMS director, Lorsch oversees $2.4 billion budget, which primarily funds basic research in the areas of cell biology, biophysics, genetics, developmental biology, pharmacology, physiology, biological chemistry, biomedical technology, bioinformatics and computational biology. NIGMS supports more than 4,600 research grants—about 11 percent of those funded by NIH as a whole—as well as a substantial amount of research training and programs designed to increase the diversity of the biomedical and behavioral research workforce.

Lorsch comes to NIGMS from the Johns Hopkins University School of Medicine, where he has been a professor in the Department of Biophysics and Biophysical Chemistry. He joined the Johns Hopkins faculty in 1999 and became a full professor in 2009.

A leader in RNA biology, Lorsch studies the initiation of translation, a major step in controlling how genes are expressed. When this process goes awry, viral infection, neurodegenerative diseases and cancer can result. To dissect the mechanics of translation initiation, Lorsch and collaborators developed a yeast-based system and a wide variety of biochemical and biophysical methods. The work also has led to efforts to control translation initiation through chemical reagents, such as drugs.

NIGMS has provided funding to Lorsch since 2000. He has also received grants from NIH’s National Institute of Diabetes and Digestive and Kidney Diseases and National Institute of Mental Health, as well as from other funding organizations.

Lorsch is as passionate about education as he is about research. During his tenure at Johns Hopkins, he helped reform the curricula for graduate and medical education, spearheaded the development of the Center for Innovation in Graduate Biomedical Education, and launched a program offering summer research experiences to local high school students, many from groups that are underrepresented in the biomedical and behavioral sciences. In addition, he advised dozens of undergraduate and graduate students and postdoctoral fellows.

Lorsch received a B.A. in chemistry from Swarthmore College in 1990 and a Ph.D. in biochemistry from Harvard University in 1995, where he worked in the laboratory of Jack Szostak, Ph.D. He conducted postdoctoral research at Stanford University in the laboratory of Daniel Herschlag, Ph.D.

Lorsch is the author of more than 60 peer-reviewed research articles, book chapters and other papers. He has also been the editor of three volumes of *Methods in Enzymology* and a reviewer for numerous scientific journals. He has one patent and one patent application related to his translation research. His honors include six teaching awards from Johns Hopkins.

Lorsch’s other activities include membership on the American Society for Biochemistry and Molecular Biology’s mentoring committee, the RNA Society’s board of directors and NIH review committees.*

*Text and photo reprinted with permission from the NIH NIGMS.
Dr. Carole L. Cramer is internationally recognized as a leader and pioneer in plant transgenics for biopharmaceutical production. She exemplifies cross-disciplinary research approaches leading to a remarkable career in translational research and biotechnology start-ups. In 2012, she was awarded the prestigious Tibbetts Award by the Small Business Administration in a ceremony at the White House. The Tibbetts Award, which is presented to small businesses and individuals that have received funding from SBIR and STTR programs, highlighted “20 years of successful SBIR research and pioneering R & D leading to the introduction of bioengineered plants for manufacturing human therapeutic proteins. Their core innovation demonstrated that the normal gene (glucocerebrosidase) for a human enzyme responsible for Gaucher’s disease could be transformed into plants and expressed to produce a bioactive human enzyme.” Dr. Cramer is an original inventor of the first FDA-approved, human enzyme replacement therapy (ERT) produced in a plant model, and in May of 2012 the drug received full FDA approval and is currently being produced and marketed for use in humans by Protalix Biotherapeutics, Inc. and Pfizer, Inc. Her current research represents the next generation of innovations in human replacement therapeutics – “hi-speed” plant expression technologies for plant-based bioproduction of complex proteins and integrated protein delivery systems that enhance therapeutic efficacy.

Dr. Cramer is currently a professor in the Department of Biology at Arkansas State University and co-founder/CSO of the biotech start-up, BioStrategies LC. She was previously on the faculty of Virginia Tech and was recruited to Arkansas to serve as founding executive director (2004 – 2010) of ASU’s Arkansas Biosciences Institute, a state-of-the-art research institute focused at the interface of agriculture and medicine. She obtained her BA in Biological Science at UC, Berkeley, her Ph.D. in Molecular Biology and Biochemistry at UC, Irvine, and her postdoctoral training at the Salk Institute.
RÉGINE DOUTHARD, M.D., M.P.H., MEDICAL OFFICER, NIGMS IDEA PROGRAM

Régine A. Douthard, M.D., M.P.H., is a medical officer in the Division of Training, Workforce Development, and Diversity, where she administers Institutional Development Award (IDeA) program grants. Before coming to NIGMS, Douthard was a medical officer in the Division of Research Infrastructure at the former National Center for Research Resources. During her tenure there, she oversaw Research Centers in Minority Institutions (RCMI) program grants. Douthard earned an M.D. from the School of Medicine and Health Sciences in Libreville, Gabon, and an M.P.H. from Emory University. She completed a residency in family practice and a fellowship in environmental and occupational medicine at the George Washington University Medical Center in Washington, D.C.

JAMES B. HOEHN, EXECUTIVE DIRECTOR, EPSCoR/IDeA FOUNDATION AND COALITION OF EPSCoR/IDeA STATES

As Director of the EPSCoR/IDeA Foundation and the Coalition of EPSCoR/IDeA States Mr. Hoehn strives to promote growth in federal, state, and local funding for science, technology, and education activities in 25 states and three territories that historically have received the least federal resources in these areas. Toward this end, Mr. Hoehn leads efforts to brief public and private sector officials who oversee higher education funding resources; prepares testimony before Congress; and meets with state Governors, university and college Presidents, non-profit leaders, business leaders, White House staff, and federal and state agency heads in order to explain the potential societal benefits of increasing academic science and education funding in all states and regions.

Mr. Hoehn was responsible for the National Science Foundation’s effort to address the geographic disparity of science and education funding resources in the United States. He chaired the EPScor Interagency Coordinating Committee which oversaw the activities of EPScor-like programs in seven federal agencies. Additionally, Mr. Hoehn was responsible for NSF’s “data gathering arm” for information related to higher education and non-profit funding in federal agencies. He oversaw congressionally-mandated studies of academic facilities and instrumentation. These studies were used to increase support for scientific research and education at NSF and other federal agencies. He was responsible for developing key metrics and benchmarks to measure national and institutional progress towards increasing funding for educational and science “equipment” and “bricks and mortar.”
ROBERT VINSON, NIH SBIR/STTR ASSISTANT PROGRAM MANAGER, NATIONAL INSTITUTES OF HEALTH, OFFICE OF THE DIRECTOR

Mr. Robert Vinson serves as an Assistant Program Manager for the National Institutes of Health (NIH) SBIR/STTR Programs in the Office of Extramural Programs, Office of Extramural Research. In this role he is responsible for providing resources to Federal staffers and access to critical information for the small business community seeking early-stage Federal funding. His duties include serving as the Contracting Officer’s Representative for the NIH Niche Assessment Program and the Commercialization Assistance Program. These programs provide technical assistance, market analysis, and commercialization guidance for NIH SBIR/STTR Phase I and Phase II awardees.

Prior to joining the SBIR/STTR Office, he was a Senior Grants Policy Analyst at the National Heart, Lung & Blood Institute (NHLBI). In that role, he managed initiatives and special projects on a variety of grants and administrative policy issues. Rob had been with NHLBI since 1993 where his career began as a Grants Management Specialist and rose to the positions of Team Leader, Grants Management Officer (GMO), and Branch Chief. Rob also served on a short detail to the Department of Health and Human Services in the Office of the National Coordinator for Health Information Technology where he was part of a cadre of GMO’s responsible for establishing Standard Operating Procedures and allocating American Recovery & Reinvestment Act funds. Additionally, for five years prior to joining NIH Rob was a commercial loan officer, with an emphasis on small business development and marketing concerns.

COMMERCIALIZATION OF BIOMEDICAL RESEARCH – PANEL DISCUSSION

The Small Business Innovation Research (SBIR) and the Small Business Technology Transfer (STTR) Programs can help move biomedical research discoveries to the marketplace. As an introduction to this panel discussion, Mr. Robert Vinson from the NIH, SBIR/STTR will give an overview of the NIH involvement in these programs. Three biomedical researchers from the Southeast Region of IDeA states will then serve as panelists and present their experiences with patenting intellectual property and carrying their discoveries in the research laboratory through the process of technology transfer to commercialization. Questions and comments are invited from the audience.

Joshua Sakon, Ph.D. is Associate Professor in the Department of Chemistry and Biochemistry at the University of Arkansas. He works as a crystallographer in the NIH/NIGMS-funded Center for Protein Structure and Function and develops drug candidates from exploration of medically important biochemistry. Currently, one of his drug candidates is licensed to BiologicsMD, Inc.

Stephen J. Cutler, Ph.D. is Professor and Chair, Department of Medicinal Chemistry, School of Pharmacy, University of Mississippi. He is also the Director of the NIH/NIGMS-funded Center of Research Excellence in Natural Products Neuroscience and has over 40 patents licensed to Garnett, LLC and Vitamar, INC. He serves as the Editor-in-Chief of Medicinal Chemistry Research, an International Journal Promoting Bioactive Compounds.

Prakash Nagarkatti, Ph.D. is Vice President for Research at the University of South Carolina and Professor in the Department of Pathology, Microbiology and Immunology in the School of Medicine. He also serves as Carolina Distinguished Professor, Director of the NIH-funded Center of Research Excellence in Inflammatory and Autoimmune Diseases (NIH/NIGMS) and a Complementary Alternative Medicine Center (NIH/NCCAM).
Scientific Sessions
1A Bioinformatics I

Location: Manning

Session Chairs: Michael Bauer, Ph.D., University of Arkansas for Medical Sciences
Eric C. Rouchka, D.Sc., University of Louisville

10:30 AM Highlight Speaker, Michael Bauer, Ph.D., University of Arkansas for Medical Sciences, Leveraging the Old with the New: Integration of Historic Microarray Studies with Next Gen Sequencing for Multiple Myeloma

11:00 AM Davida Crossley, Alcorn State University, Characterizing the Function of the M46 Gene in the Pathogenic Fungus Histoplasma capsulatum

11:15 AM Sarah M. Schrader, Western Kentucky University, Bioinformatic Analysis of Mycobacteriophage TiroTheta9

11:30 AM Devaun McFarland, University of South Carolina, Utility of msTALI in Protein Active Site Identification

11:45 AM Erich Peterson, University of Arkansas for Medical Sciences, Variant Consensus Reporter: Increasing the Confidence of Variants in Whole Exome Sequencing via a Consensus Approach

1B Cancer I

Location: Salon A

Session Chairs: Scott Weed, Ph.D., West Virginia University
Lori Hensley, Ph.D., Ouachita Baptist University, Arkansas

10:30 AM Highlight Speaker, Seetharama Satyanarayanajois, Ph.D., University of Louisiana at Monroe, EGFR heterodimerization: Dynamics, docking and inhibition of signaling for breast, lung and ovarian cancer

11:00 AM Stuart Grimes, Clemson University, Nanoparticle Delivery of Non-Toxic Drugs to Enhance the Efficacy of Chemotherapeutic Drugs

11:15 AM Greg Phelps, Arkansas State University, Effects of Ionizing Radiation on Guanine Triphosphate Cyclohydrolase 1 Activity

11:30 AM Lori L. Hensley, Ph.D., Ouachita Baptist University, Antitumor effects of the synthetic cannabinoid ajulemic acid on Ewing’s sarcoma

11:45 AM Donald J. Johann, Jr., Ph.D., University of Arkansas for Medical Sciences, Towards computer assisted laser microdissection
1C Cardiovascular Research

Location: Arkansas Ballroom

Session Chairs: Daniel R. Kapusta, Ph.D., Louisiana State University
Dakota Pouncey, Hendrix College

10:30 AM Highlight Speaker, Minolfa C. Prieto, M.D., Ph.D., Tulane University, School of Medicine, *Deletion of prorenin receptor in the collecting duct attenuates blood pressure in angiotensin II hypertensive mice*

11:00 AM Dakota Pouncey, Hendrix College, *Identifying Potential R/S-Warfarin Metabolite Biomarkers to Improve Anticoagulant Dosing Strategies in Children*

11:15 AM Rachel N Stamp-Siegfried, University of Arkansas for Medical Sciences, College of Medicine, *Effects of Daily Kangaroo Care on Cardiorespiratory Parameters in Preterm Infants*

11:30 AM Sarah Bishop, Ouachita Baptist University, *Protective effects of aqueous extract of Terminalia arjuna bark against doxorubicin-induced cardiotoxicity*

11:45 AM Nalini Santanam, Ph.D., MPH, Joan C. Edwards School of Medicine, Marshall University, *Perivascular Fat Relation to Hypertension and Coronary Artery Disease*

1D Cell Signalling

Location: Hoffman

Session Chairs: Emilia Galperin, Ph.D., University of Kentucky
Helen Beneš, Ph.D., University of Arkansas for Medical Sciences

10:30 AM Highlight Speaker, Guo-Lei Zhou, Ph.D., Arkansas State University, *GSK3 phosphorylates the actin regulatory protein CAP1 to control the actin cytoskeleton and cell polarization*

11:00 AM Timothy M. Horton, Ouachita Baptist University, *Inhibiting recognition of the B-cell receptor by the tyrosine kinase Syk*

11:15 AM James A. Stahl, University of Arkansas for Medical Sciences, *Global phosphoproteomic analyses define host signaling networks usurped for gammaherpesvirus replication*

11:30 AM Jeffrey Sifford, University of Arkansas for Medical Sciences, *Productive MHV68 infection compromises the cellular p53 signaling pathway*

11:45 AM Emilia Galperin, University of Kentucky, *HUWE1 is a molecular link controlling RAF-1 activity supported by the Shoc2 scaffold*
2A General Biomedical Sciences

Location: Hoffman

Session Chairs: 
  Angus MacNicol, Ph.D., University of Arkansas for Medical Sciences
  Stephanie Byrum, Ph.D., University of Arkansas for Medical Sciences

2:45 PM 
  Highlight Speaker, Jeffrey Anker, Ph.D., Clemson University, Luminescent sensing and imaging through tissue

3:15 PM 
  Angus MacNicol, Ph.D., University of Arkansas for Medical Sciences, A Novel Bioassay to Identify Chemical Regulators of Stem Cell Self-Renewal

3:30 PM 
  Dustin Walter, Ouachita Baptist University, A Radial Diffusion Assay for the Rapid Evaluation of Antimicrobial Peptides

3:45 PM 
  Ameya S Gokhale, University of Louisiana Monroe, Surface epitopes of CD2 protein to inhibit CD2-CD58 protein-protein interaction as therapeutic agent for arthritis

4:00 PM 
  Stephanie Byrum, Ph.D., University of Arkansas for Medical Sciences, Purification of a Specific Native Genomic Locus for Proteomic Analysis

2B Infectious Disease/Immunology I

Location: Manning

Session Chairs: 
  Gus Konsoulas, Ph.D., Louisiana State University
  Karl Boehme, Ph.D., University of Arkansas for Medical Sciences

2:45 PM 
  Highlight Speaker, Sanjay Batra, Ph.D., Louisiana State University, Lipid rafts influence the formation of immunoproteasomes via RIP2/NLR pathway against Klebsiella pneumoniae

3:15 PM 
  Carrie S. Yang, Hendrix College, Ibrutinib, a potential treatment for chronic Graft versus Host Disease inhibits T-helper 17 activation and release of IL-17A

3:30 PM 
  Eduardo Salinas, University of Arkansas for Medical Sciences, Enhancement of Gammaherpesvirus Productive Infection by TRIM21 as Revealed through a Proteomics-based LANA Interaction Screen

3:45 PM 
  Yun Xiang, Clemson University, A quantitative evaluation of the binding affinity between antibody decorated liposomes and the antigen using SPR

4:00 PM 
  Logan Blancett, The University of Southern Mississippi, Characterization of the nitrogen regulatory protein AREA in the dimorphic fungus Histoplasma capsulatum
2C Neuroscience

Location: Salon A

Session Chairs: Robert Doerksen, Ph.D., University of Mississippi
               Melanie MacNicol, Ph.D., University of Arkansas for Medical Sciences

2:45 PM   Highlight Speaker, Melanie C. MacNicol, Ph.D., University of Arkansas for Medical Science, *Control of neural stem cell differentiation and survival through manipulation of Musashi-mediated mRNA translation*

3:15 PM   Mahmoud Kiaei, Ph.D., University of Arkansas for Medical Sciences, *Nrf2 Activation as Novel Therapeutic Strategy for ALS and its Neuroprotective Mechanisms in Astrocytes and Motor Neurons*

3:30 PM   Miki S. Lindsey, University of Central Arkansas, *Calpain Inhibition Blocks Tributyltin Induced Neurodegeneration*

3:45 PM   Pankaj Pandey, University of Mississippi, *Utilizing the ensemble docking method for ranking and selection of representative cannabinoid receptor subtype 2 (CB2) models*

4:00 PM   Julie Stenken, Ph.D., University of Arkansas, *Microdialysis Sampling of Cytokine Cell Signaling Proteins in Neuroscience and Wound Healing Applications*

2D Undergraduate Research

Location: Arkansas Ballroom

Session Chairs: Marty Perry, Ph.D., Ouachita Baptist University, Arkansas
                Tim Horton, Ouachita Baptist University, Arkansas

2:45 PM   John Butler and Kirby Von Edwins, Cell Signalling, Ouachita Baptist University, *A Comparative Genomics Approach to Link Plant and Animal Oxidative Stress Signaling Pathways*

3:15 PM   Jennifer Greene, General Biomedical Sciences, University of Charleston, WV, *Analysis of polymeric gels for the transdermal delivery of capsaicin for the treatment of chronic low back pain*

3:30 PM   Amy Ni, Neuroscience, Western Kentucky University, *Time-course of effects of growth hormone (GH) and GH antagonist on auditory hair cell regeneration in zebra fish (Danio rerio)*

3:45 PM   Boyang Piao, Infectious Disease/Immunology, Louisiana State University, *Understanding the mucus production of a human respiratory paramyxovirus infection (ID24)*

4:00 PM   Franshawn Mack, Cancer, South Carolina State University, *Evaluating the Reliability of the ARTQ in Assessing Cancer Clinical Trial Perceptions in a Predominantly Black Sample in SC*
3A Bioinformatics II

Location: Hoffman

Session Chairs: Glen Shearer, Ph.D., University of Southern Mississippi
Somdutta Saha, University of Arkansas for Medical Sciences

10:00 AM C. Stephen Embry, University of Arkansas at Little Rock/University of Arkansas for Medical Sciences, NeedleAnalyzer: A Data Analysis Tool for LCMS-Based Untargeted Metabolomics Data

10:15 AM Arjang Fahim, University of South Carolina, nDh-PDPA: n-Dimensional Hybrid Probability Density Profile Analysis

10:30 AM Somdutta Saha, University of Arkansas for Medical Sciences/University of Arkansas at Little Rock, Defining the Recognition Elements of Lewis Y-Reactive Antibodies

10:45 AM Katelyn Robillard, Southeastern Louisiana University, Investigation of the Mechanism of Apparent HPLC Solvent Interference with an Avidin-Binding Assay

11:00 AM Mihir Jaiswal, University of Arkansas Little Rock/University of Arkansas for Medical Sciences, XLPM: X-linked Peptide Mapping Algorithm

11:15 AM Nathan Crabtree, University of Arkansas Little Rock/University of Arkansas for Medical Sciences, Adapting a computational evolution system to the analysis of RNA-Seq treatment/response differential gene expression data

3B Cancer II

Location: Salon A

Session Chairs: Karen Martin, Ph.D., West Virginia University
Joshua Sakon, Ph.D., University of Arkansas

10:00 AM Highlight Speaker, Jorge I. Rodriguez-Dévora, Ph.D., Clemson University, Miniaturized Bioprinting Platform for Personalized Cancer Therapy

10:30 AM Scott A. Weed, West Virginia University, Monitoring changes in cervical lymph nodes by high-frequency ultrasound in a 4-NQO mouse model of oral cancer

10:45 AM Laura Strossner, Ouachita Baptist University, Creating Model Systems to Study the Effects of Ajulemic Acid on Solid Pediatric Tumors

11:00 AM Shweta Chavan, Ph.D., University of Arkansas for Medical Sciences, Profiling Multiple Myeloma Engraftment Phenomena via an in-vivo SCID Mouse Model and RNA-seq

11:15 AM Joshua Sakon, Ph.D., University of Arkansas, Targeting mechanism of prototypical collagen binding domains from clostridial collagenase
3C Infectious Disease/Immunology II

Location: Manning

Session Chairs:  
Mark Smeltzer, Ph.D., University of Arkansas for the Medical Sciences
Ahmad Saied, Louisiana State University

10:00 AM  
Highlight Speaker, Antonieta Guerrero-Plata, Ph.D., Louisiana State University, *Type III interferon response by respiratory paramyxovirus infection*

10:30 AM  
Jason S. Stumhofer, University of Arkansas for the Medical Sciences, *ICOS-mediated Tfh cell differentiation during Plasmodium chabaudi infection*

10:45 AM  
Ahmad Saied, Louisiana State University, *Functional Hierarchy of HSV-1 Membrane Proteins in Corneal Infection and Virus Transmission to Ganglionic Neurons*

11:00 AM  
Brent Stanfield, Louisiana State University, *Vaccination with the HSV-1 Attenuated Virus VC2 Protects Mice against Lethal Challenge with Virulent HSV-1 and HSV-2 strains*

11:15 AM  
Gyan S. Sahukhal, University of Southern Mississippi, *Defining a New Operon, msa, and its Role in Biofilm Development and Virulence*

---

Men love to wonder, and that is the seed of science.  
Ralph Waldo Emerson
Scientific Session Abstracts
BIO1  Leveraging the Old with the New: Integration of Historic Microarray Studies with Next Gen Sequencing for Multiple Myeloma

Michael Bauer, Ph.D.
Post Doctoral Fellow, University of Arkansas for Medical Sciences
djjohann@uams.edu

Michael Bauer, Ph.D., Erich Peterson1, Shweta Chavan1, Daniel Pollock1, Christoph J. Heuck1, Donald J. Johann, Jr.1 1Myeloma Institute for Research and Therapy, University of Arkansas for Medical Sciences, Little Rock, AR

Next Gen Sequencing (NGS) methods are disruptive and are rapidly providing remarkable advances in our ability to study the molecular profiles of human cancers. However, the scientific discovery offered by NGS also includes challenges concerning the interpretation of large and non-trivial experimental results. This task is potentially further complicated when a multitude of molecular profiling modalities are available, with the goal of a more integrative type analysis of the cancer biology. As technology advances, it is critical to leverage what has been gained from historic approaches (e.g., microarrays) to new approaches (NGS). Microarray transcriptome analyses have resulted in important advances in biomedicine. For instance in multiple myeloma (MM), microarray approaches led to the development of a prognostic 70 gene risk score as well as an effective disease subtyping via cluster assignment. Both enabled an improved molecular understanding of MM, and have provided translational information for the purposes of more advanced patient management. Today, many researchers are transitioning to NGS DNA approaches for the detection of sequence variants, as well as RNA-seq, also due to its discovery-based nature, improved sensitivity, and dynamic range. Utilizing a model-view-controller (MVC) approach, a suite of custom software tools have been developed to integrate NGS experimental data along with microarray and Affymetrix probe set-IDs, and gene annotation information from a variety of public sources. The approach employs a variety of strategies to integrate, annotate, and associate microarray and NGS datasets. Output from the Tuxedo suite and GATK can be directly integrated, and/or associated with microarray and Affymetrix probe set data, as well as necessary gene identifiers and/or symbols from a variety of sources. Illustrated will be strategies employed to maximize the integration and annotation processes across molecular profiling modalities for MM.

BIO2  Characterizing The Function of the M46 Gene In The Pathogenic Fungus Histoplasma capsulatum

Davida Crossley, Ph.D.
Assistant Professor, Alcorn State University
dcrossley@alcorn.edu

Davida Crossley, Ph.D., Glenmore Shearer The University of Southern Mississippi

Histoplasma capsulatum (Hc), is the etiologic agent for the respiratory infection histoplasmosis. The dimorphic fungus exists in the soil as a multi-cellular saprophytic mold, and converts to a uni-cellular parasitic yeast in the mammalian host. The conversion to the yeast morphotype is a requirement for pathogenesis. Mold and yeast phase specific genes have been of interest, particularly with finding genes that are involved in dimorphism. M46, is a mold specific gene with no significant homologs according to NCBI Genbank, and therefore the function of M46 is unknown. Disruption of the M46 gene by allelic replacement, showed that M46 is not involved in dimorphism or maintaining normal mycelial growth rate. In this study, parallel comparison of gene expression of the M46 knockout and native strain was conducted by using RNA sequencing. Scatter plot representation of gene expression show that ~500 genes were differentially expressed amongst the two strains. Ontology reports, by using the computer software program Blast2 go, showed that the down regulation of M46, caused an increase of gene expression in 33 genes that were involved in transport. Eleven of the transporters were part of the Major Facilitated Super Family (MFS). Six of these MFS transporters, were correlated with the drug efflux system. These results, suggests that M46 may be involved in drug resistance. Current work focuses on identifying the anti-fungal substrates for the MFS transporters and conducting drug susceptibility assays.
Bioinformatic Analysis of Mycobacteriophage TiroTheta9

Sarah M. Schrader
Undergraduate Student, Western Kentucky University
sarah.schrader435@topper.wku.edu

Sarah M. Schrader, Rodney A. King and Claire A. Rinehart, Western Kentucky University

Bacteriophages are the most abundant biological entities on Earth, yet relatively few have been characterized. We isolated and characterized a novel bacteriophage from the environment and compared its physical and genetic features with others in the databases. Mycobacterium smegmatis, a harmless soil bacterium, served as the host and facilitated the enrichment and recovery of mycobacteriophages. A single phage type was purified to homogeneity and was named TiroTheta9 (TT9). Electron microscopy revealed that the phage particles have hexagonal heads that are 54 nm in diameter, and tails that are 160 nm in length. The TT9 genomic DNA was purified and sequenced using 454 pyrosequencing technology. The 51,355 bp genome contains 79 genes that were identified using the gene prediction programs Glimmer and Genemark. However, only 24 genes could be assigned functions based on BLAST analysis. Genome wide comparisons using the Phamerator program revealed that TT9 is most closely related to members of the A4 subcluster of mycobacteriophages. Although all A4 subcluster phages have been isolated from geographically distinct locations, their genomic sequences are highly conserved. Our results have contributed to the rapidly expanding database of mycobacteriophage genomes. Mining this rich source of genetic information should provide new insights into phage diversity and evolution.

Utility of msTALI in Protein Active Site Identification

Devaun McFarland
Graduate Student, University of South Carolina
mcfarlad@email.sc.edu

Devaun McFarland, Homayoun Valafar Department of Computer Science and Engineering, University of South Carolina

With the profusion of protein sequence and structure data, it’s increasingly relevant to develop automated methods of identifying and investigating protein active sites. Site identification will have a direct impact: in stronger understanding the molecular basis for diseases, assisting in drug design, the study of targeting mutants, the functional annotation of unknown proteins, and provide beneficial information for protein design and engineering. Existing computational approaches to active-site identification fall short of ideal by failing to include some critical information such as: global structure, local structure, amino acid position, and local biochemical properties. Here we present msTALI (Multiple Structure Torsion Angle Alignment) as a method to better understand and characterize protein sequence-structure-function relationships. The existing studies establishing our understanding of active sites stress the importance of sequence, structure, and biochemical properties of proteins in their function. msTALI is an ideal method for active site analysis since all the aforementioned information is considered. Preliminary results indicate that msTALI generates competitive results which exhibit an ability to address proteins undergoing rigid-body motion. This application of msTALI is in study of ATPase active site identification. We report the results of msTALI in this application compared to results previously obtained using the CO (Continuous Optimization) and MolLOC (Molecular Local surface comparison) methods. We first report the results of pairwise comparisons on an initial dataset of 19 proteins, from previous study, with confirmed ATPase activity and the confirmed binding sites. In this regard, our initial investigations demonstrate a far more superior result by observing a higher number of aligned atoms and a lower RMSD. Finally, we produce simultaneous alignments for all structures – a feature unique to msTALI – to produce more meaningful results.
BI05  Variant Consensus Reporter: Increasing the Confidence of Variants in Whole Exome Sequencing via a Consensus Approach

Erich Peterson, Ph.D.
Post Doctoral Fellow, University of Arkansas for Medical Sciences
djohann@uams.edu

Erich Peterson, Ph.D., Shweta S. Chavan, Michael A. Bauer, Christoph Heuck, Donald J. Johann, Jr. Myeloma Institute for Research and Therapy, University of Arkansas for Medical Sciences, Little Rock, AR

Introduction: Several tools now exist for the calling of variants from data produced by high throughput sequencing technologies. These tools, such as GATK and others, in conjunction with functional annotation tools, offer the promise of narrowing down the search for variants, which may directly affect a patient’s cancer biology. However, more complex variants typically rely heavily on statistical models, and various approaches use differing algorithmic techniques. Thus, determining which tool’s called variants may have the necessary confidence warranting further experimental validation can be tricky. Here we present an approach, called the Variant Consensus Reporter, for culling variants from several variant calling tools using a consensus method. The result is a report that can give the investigator more information and confidence concerning identified variants. Methods DNA from the Multiple Myeloma (MM) cell lines, RPMI-8226 and U266 BZ, were extracted and prepared for whole exome sequencing (WES) on an Illumina HiSeq 2500. A standardized computational pipeline for DNA processing has been designed and developed. In brief, it provides uniform methods and relies on BWA and STAMPY for alignment and BAM file creation. Variant calling is performed utilizing GATK as well as other methods, which result in a Variant Call File (VCF). Those VCFs were additionally functionally annotated using ANNOVAR. Finally, the two VCF files were used as input for the Variant Consensus Reporter, which analyzes the variant calls produced by each tool to create a consensus report. Results As a test-case, the Variant Consensus Reporter was designed and developed to report consensus variants, which contain the following functional annotations: i) Point mutations (both missense and nonsense); ii) Frame-shift mutations. These particular annotated variants were chosen because of their potential to be clinically actionable.

Cancer I Session 1B

CN01  EGFR heterodimerization: Dynamics, docking and inhibition of signaling for breast, lung and ovarian cancer

Seetharama SatyanarayanaJois, Ph.D.
Associate Professor, University of Louisiana at Monroe
jois@ulm.edu

Seetharama SatyanarayanaJois, Shanthi Kanthala, Yong-Yu Liu University of Louisiana at Monroe

Epidermal growth factor receptors (EGFRs) belong to the transmembrane receptor tyrosine kinase (RTK) family of receptors that mediate cell signaling resulting in cell growth, differentiation and motility. Once the signal transduction mechanism is achieved, in normal cells activation of receptors is attenuated by mechanisms such as receptor internalization and downregulation. Deregulation of signaling due to mutation of the receptors and constitutive activation as well as dimerization has been reported in several types of cancers. HER2 is overexpressed in 20-30% of breast cancer. Apart from breast cancer, HER2 is also overexpressed in ovarian and lung cancer. HER2 is known to exist in always open conformation without any known ligand and is the preferred partner among EGFRs for homo and heterodimerization which is stabilized by Protein-Protein interactions (PPI) of extracellular domain II and domain IV which leads to signaling. Domain IV of HER2 is a clinically validated target by antibody trastuzumab. Here we investigated the PPI of domain IV using molecular dynamics approach. Heterodimers of EGFRs were built using available crystal structure and subjected to nanosecond M.D. simulation using NAMD software. Furthermore, the dimerization of EGFRs was inhibited by design of peptidomimetics. Docking studies were performed to understand the interaction of peptidomimetics with HER2 protein and a model for PPI inhibition of EGFRs was proposed. Inhibition of dimerization was evaluated using pathhunter assay, proximity ligation assay and western blot analysis and correlated with antiproliferative activity against breast, ovarian and lung cancer cell lines. The lead peptidomimetics were evaluated for their ability to suppress breast cancer tumor using a xenograft model of breast cancer. This project was supported by the National Institutes of Health through the National Institute of General Medical Sciences Grant 8P20GM103424 via Louisiana Biomedical Research Network program.
**CN02** Nanoparticle Delivery of Non-Toxic Drugs to Enhance the Efficacy of Chemotherapeutic Drugs

Stuart Grimes  
Graduate Student, Clemson University  
falexis@clemson.edu

Stuart Grimes, Jhilmil Dhulekar, Thomas Moore, Olivia Decroes, Ian Hale, Charles Laughlin, Frank Alexis

The development of chemotherapeutic loaded polymeric nanoparticles for the treatment of solid tumors is a rapidly growing area of study in nanomedicine as it carries the potential to vastly improve the efficacy of cancer therapy. Solid tumors, such as those of glioblastomas or neuroblastomas, can be passively targeted by the therapeutic nanoparticles when injected into circulation in the body due to the enhanced permeability and retention effect (EPR), which these specific tumors display. The major advantages of encapsulating a drug in polymeric nanocarriers and delivery of these nanoparticles to specific cells include a sustained drug release to the tumor, enhanced targeting capabilities, and reduced side effects to healthy tissue. Here, a non-toxic agent is being studied as a possible chemotherapeutic drug in nanoparticles to be administered in combination with a free toxic drug for the treatment of solid tumors. The specific non-toxic drug in this study has been shown to increase the effect of the toxic chemotherapeutic when administered together. By loading polymeric nanoparticles with this non-toxic therapeutic agent, it is possible to deliver and treat the specific tumor cells for an extended period of time so that the toxic drug has an increased effect. In vitro studies have shown that the non toxic drug has minimal toxic effects on several cancerous cell lines, while demonstrating improved cytotoxic effects of the toxic drug when both are administered in combination. Future goals of this study will focus on attaching a targeting ligand to further enhance the uptake of drug loaded nanoparticles and direct targeting of the specific cancer cells.

**CN03** Effects of Ionizing Radiation on Guanine Triphosphate Cyclohydrolase 1 Activity

Greg Phelps  
Undergraduate Student, Arkansas State University  
gregory.phelps@smail.astate.edu

Greg Phelps, Rupak Pathak and Howard Hendrickson University of Arkansas for Medical Sciences

Ionizing radiation therapy is known for its usefulness in cancer treatment, but its long-term adverse effects in patients are also well known. Radiation has many harmful effects on the body including endothelial dysfunction, which is believed to be dependent on the amount of NO present. The pathway which is thought to be responsible for this is the biopterin pathway. Along the pathway, Guanine Triphosphate Cyclohydrolase 1 (GTPCH1) is the first and rate-limiting enzyme in the production of tetrahydrobiopterin (BH4). When there are low levels of this enzyme or it is regulated by Guanine Triphosphate Cyclohydrolase Feedback Regulatory Protein (GFRP) there is not enough GTPCH 1 available to keep up with the minimum amount of BH4 required by the body. BH4 is an essential co-substrate for the NOS systems and in this case, when things go as expected NOS produces NO, but if there is a BH4 deficiency, it catalyzes the production of superoxide instead of NO, which can lead to cell damage. In this study, we look to determine if the cause of this dysfunction is changes to GTPCH1 activity using experimental procedures (GTPCH1 assay) to isolate and measure the levels of activity of this enzyme in mice tissue that has been exposed to ionizing radiation and up regulated GFRP. Following incubation with GTP the reaction was quenched and BH4 chemically converted to neopterin. HPLC with fluorescence detection was used to determine the amount of the neopterin produced. In this study, we hope to recognize GTPCH 1 activity as biomarker of radiation injury and later on, develop a drug or treatment that might prevent or reverse the effects of radiation injury resulting from radiation treatment for cancer, accidental radiation exposure, or possible terrorism event.
CN04  Antitumor effects of the synthetic cannabinoid ajulemic acid on Ewing's sarcoma

Lori L. Hensley, Ph.D.
Associate Professor, Ouachita Baptist University, Arkansas
hensleyl@obu.edu

Lori L. Hensley, Amy G. Eubanks (1), Joseph Levy (1,2), Nathan Koonce (2), Jessica Webber (2), Drake C. Hardy (1), Laura E. Strossner (1), Michael L. Sullivan (1), and Robert J. Griffin (2) (1) Ouachita Baptist University, Department of Biology (2) UAMS, Department of Radiation Oncology

Ewing's sarcoma is a pediatric bone cancer that is highly aggressive, leading to a five-year survival rate of less than 30%, even with multi-modal treatment protocols. Improved therapeutic options are desperately needed. Our research, completed primarily by undergraduate students, has focused on the abilities of ajulemic acid, a nonpsychoactive cannabinoid, to decrease hallmarks of tumorigenicity. Our data show that ajulemic acid can successfully decrease cell viability through the induction of apoptosis, decrease tumor and endothelial cell migratory capacities, and inhibit angiogenesis in in vitro model systems. We have also developed a bioluminescent mouse model to test the efficacy of ajulemic acid against tumor cells in an in vivo system. In this model, luciferase-expressing tumor cells are injected into the tibiae of mice and the growth or regression of tumors in control and treated mice is tracked. Using this murine model, we demonstrate that tumors can be induced to grow in the bone and will metastasize to the lungs, mimicking the human disease. We hypothesize that these experiments provide the basis for the development of cannabinoid-based therapies for this devastating family of cancers.

CN05  Towards computer assisted laser microdissection

Donald J. Johann, Jr., Ph.D.
Associate Professor, University of Arkansas for Medical Sciences
djohann@uams.edu

Donald J. Johann, Jr., Liang Zhang, Erich Peterson Myeloma Institute for Research and Therapy, University of Arkansas for Medical Sciences, Little Rock, AR

Laser-based tissue microdissection facilitates the isolation of cell populations from clinical or animal model specimens based on visual selection by a human operator. Although a successful research method, laser dissection can be a tedious and time-consuming undertaking when large numbers of the specific cells of interest are needed for subsequent molecular analysis. For instance, several thousand cells (e.g., 3,000 to 15,000) are commonly required for molecular profiling studies utilizing shotgun proteomics or a next generation sequencing (NGS) type experiments. Additionally and quite importantly, the tumor proper and microenvironment are many times best analyzed separately. This is relevant since many new drugs are now designed to target the microenvironment (e.g., angiogenesis inhibitors) or a specific target on the tumor (e.g., the monoclonal antibody trastuzumab targeting the HER2/neu receptor in breast cancer). Hence, the ability to collect cells from different regions of a solid tissue sample and then analyze them separately is essential to the specificity of the findings. In this regard, computer-aided laser dissection (CALD) is a new approach that integrates digital imaging and pattern recognition algorithms into the process to significantly extend and improve capabilities. This approach permits the computer algorithm to identify cells of interest, followed by a “more programmed” microdissection, allowing the operator to act as a supervisor, and thus providing automation to a frequently laborious process. Since there are four major manufactures of laser dissection instruments, there is consideration for appropriate interfacing strategies. This may allow for a component or template type approach, which can serve to foster a plug-and-play approach for pattern matching algorithms, as well as towards CALD in both research and clinically oriented workflows. Efforts toward these aims will be illustrated.
CV01  Deletion of prorenin receptor in the collecting duct attenuates blood pressure in angiotensin II hypertensive mice

Minolfa C. Prieto, M.D., Ph.D.
Assistant Professor, Tulane University, School of Medicine
mprieto@tulane.edu

Minolfa C. Prieto, M.D., Ph.D., Camille Bourgeois, Alex Castillo, and L Gabriel Navar,  Department of Physiology and Renal Hypertension Center of Excellence, Tulane University, School of Medicine

Prorenin is synthesized and secreted in the principal cells of the collecting duct. In this nephron segment, the prorenin receptor (PRR), a specific receptor for renin and prorenin, is expressed in the intercalated cells. In vitro evidence suggests that PRR activates prorenin and enhances the activity of renin. The augmented expression of PRR in the kidneys of animal models of hypertension and diabetes raises the possibility whether binding of PRR to collecting duct derived-prorenin augments intratubular renin activity and the potential for Ang II generation. To examine the in vivo relevance of the functional role of PRR on the enhancement of activity of renin-derived from the collecting duct, we generated mice with cell type specific deletion of the PRR in this nephron segment. To delete the PRR gene (Atp6ap2) from the intercalated cells, we used mice with a conditional floxed Atp6ap2 allele (Atp6ap2floxflox), generated and provided by Dr. Atzuhiro Ichihara (Japan), which were bred with transgenic mice for the Hoxb7 promoter driving expression of Cre-recombinase (Hoxb7-Cre). In this nephron segment, PRR is only expressed by the intercalated cells but not by the principal cells. RNA analysis confirmed kidney-specific recombination, and medullary PRR mRNA levels were decreased 3-fold in cdPRR-KO mice. Blood pressure (BP) was recorded by telemetry and plasma and urine was collected in 24-hour metabolic cages on normal, high-, and low-Na+ diets. No significant differences were observed in 24-hour urinary Na+ excretion. Furthermore cdPRR-KO mice subjected to chronic Ang II infusions (400 ng/min for 14 days) showed attenuation of BP compared with Ang II-infused mice on a high-Na+ diet. Ren activity was 2-fold lower in urines from targeted mice as compared with controls. These results indicate this model is a suitable tool to demonstrate the critical role of activation of prorenin by the PRR in the collecting duct in hypertension and diabetes.

CV02  Identifying Potential R/S-Warfarin Metabolite Biomarkers to Improve Anticoagulant Dosing Strategies in Children

Dakota Pouncey
Undergraduate Student, Hendrix College
Pounceyd@gmail.com

Dakota Pouncey, C. Preston Pugh2, Drew R. Jones2, Gunnar Boysen3, Kathleen Neville4, and Grover P. Miller2 2 Department of Biochemistry and Molecular Biology, University of Arkansas for Medical Sciences, Little Rock, AR 3 College of Public Health, University of Arkansas for Medical Sciences, Little Rock, AR 4 Children’s Mercy Hospital, Kansas City, MO

Coumadin (R/S-warfarin) is an anticoagulant drug marketed globally to manage thromboembolic events. Warfarin therapy is very effective, but remains challenging as a result of a narrow therapeutic range and high inter-individual variations in response to treatment. While most warfarin therapy data corresponds to adults, optimal pediatric dosing is significantly different and further complicates treatment in children. Therefore, it is critical to develop ways to improve pediatric warfarin therapy. We hypothesize that metabolite profiles in plasma can be used to predict a safe and effective warfarin therapy based on the results of a single blood test. In a preliminary study, we determined metabolite profiles of R/S-warfarin metabolites for eight pediatric patient plasma samples through the UAMS Metabolomics Core Facility. The patient medical histories were analyzed to determine three clinical outcomes of each individual: (1) time to achieve stable therapeutic response; (2) warfarin dosage to maintain stable therapeutic response; and (3) percent time out of therapeutic response. We then employed a simple Pearson correlation analysis to identify correlations among metabolic pathways to better understand the underlying mechanisms of warfarin metabolism. Secondly, we identified correlations between metabolic pathways and clinical outcomes to identify metabolite biomarkers that could be used to predict patient response. Correlations between metabolites offered insight into the enzymatic pathways responsible for their formation and correlations between metabolites and clinical outcomes identified potential biomarkers of adverse outcomes. We also found that changes in CYP2C9 activity may be compensated by CYP3A4, possibly influencing warfarin dosing and drug-drug interactions. A larger sample set in future studies will reveal more reliable predictors of patient dose responses to warfarin therapy.
CV03 Effects of Daily Kangaroo Care on Cardiorespiratory Parameters in Preterm Infants

Rachel N Stamp-Siegfried
Graduate Student, University of Arkansas for Medical Sciences, College of Medicine
RStampSiegfried@uams.edu

Rachel N. Stamp-Siegfried, Anita J Mitchell, Ph.D., APN University of Arkansas for Medical Sciences, College of Nursing
Charlotte Yates, Ph.D., PT University of Central Arkansas, Department of Physical Therapy
Keith Williams, Ph.D. University of Arkansas for Medical Sciences, College of Medicine, Department of Biostatistics
Richard W Hall, M.D. University of Arkansas for Medical Sciences, College of Medicine, Department of Pediatrics and Neonatology

Background/aims: Kangaroo care (KC) has possible benefits for promoting physiological stability and positive developmental outcomes in preterm infants. The purpose of this study was to compare bradycardia and desaturation events in preterm infants in standard incubator care (SC) versus KC. Methods: Thirty-eight infants 27 to 30 weeks gestational age were randomly assigned to 2 hours of KC daily between days of life (DOL) 5 to 10 or to continuous SC. Infants were monitored for bradycardia (heart rate <80) or oxygen desaturation (<80%). Analysis of hourly events was based on three sets of data: SC group 24 hours daily, KC group during incubator time 22 hours daily, and KC group during holding time 2 hours daily. Results: The KC group had fewer bradycardia events per hour while being held compared to time spent in an incubator (p=0.048). The KC group also had significantly fewer oxygen desaturation events while being held than while in the incubator (p=0.017) and significantly fewer desaturation events (p=0.0015) than infants in standard care. Conclusion: KC reduces bradycardia and oxygen desaturation events in preterm infants, providing physiological stability and possible benefits for neurodevelopmental outcomes. Long-term benefits of KC should be determined by future research. Additional research may verify our hypothesis that the angle of KC decreases obstructive apnea. Further research using high-resolution monitors that incorporate software designed to define apnea, bradycardia, and oxygen desaturation events should be done to determine any associations between these events.

CV04 Protective effects of aqueous extract of Terminalia arjuna bark against doxorubicin-induced cardiotoxicity

Sarah Bishop
Undergraduate Student, Ouachita Baptist University, Arkansas
bis48801@obu.edu

Sarah Bishop, Shi Liu Department of Pharmaceutical Sciences, College of Pharmacy, University of Arkansas for Medical Sciences

The bark of Terminalia arjuna (TA), a tropical tree, has been used in Ayurvedic medicine for treatment of cardiovascular disease. TA bark is known to contain various antioxidants, and recently it has been suggested to enhance function of the normal heart as an over-the-counter supplement in the USA. The mechanism underlying cardiac actions of TA bark are unknown. Doxorubicin (DOX), a commonly-used anticancer drug, is known to cause cardiotoxicity, a major concern in chemotherapy. The aim of this study is to investigate if aqueous extracts of TA bark (TAaq) protect the heart from DOX treatment by counteracting the oxidative stress caused by DOX. Cardiac function of mice with and without co-treatment of DOX and TAaq was monitored by weekly echocardiography. H9c2 cells, a cell line derived from the heart, were used for the in vitro study to examine possible mechanism(s) of TAaq. Our in vivo data showed that TAaq (100 μg/ml in drinking water) abolished the decrease in left ventricle function caused by multiple weekly treatment with DOX. In vitro data showed that treatment with DOX (1 μM, for 24 hr) increased superoxide production and damage to the growth network of H9c2 cells, which were attenuated by co-treatment with TAaq (100 μg/ml). These preliminary data suggest that TAaq protect the heart in part from oxidative stress caused by DOX. The involved signaling pathways will be investigated in the future study.
CV05 Perivascular Fat Relation to Hypertension and Coronary Artery Disease

Nalini Santanam, Ph.D., MPH
Professor, Joan C. Edwards School of Medicine, Marshall University, Huntington, WV
santanam@marshall.edu

Nalini Santanam, Ph.D., MPH, Christopher Adams, M.D.; Nepal Chowdhury, M.D.; Todd Gress, M.D.; Paulette Wehner, M.D.; Carla Cook, BS; Department of Pharmacology, Physiology, Toxicology, Department of Medicine (Cardiology), Department of Thoracic Surgery, Joan C Edwards School of Medicine, Marshall University, Huntington, WV.

Obesity levels have increased alarmingly in the Appalachian Region. This has resulted in an increase in the incidence of hypertension, hyperlipidemia and Type 2 diabetes in this region. Adipose tissue plays an important role in these diseases. Perivascular fat (PVF) that surrounds the heart and vasculature has an immediate paracrine and autocrine effect on cardiac and vascular function. Increase in body weight increases both PVF size and inflammatory milieu, thereby altering its ability to regulate vascular function. Anti-contractile factors released by PVF plays a role in vasodilation. The identity of these PVF derived anti-contractile factors and its role in hypertension is not well understood. The objective of this study was to investigate if changes in PVF size and secreted factors correlate with presence of hypertension in patients undergoing coronary artery bypass graft (CABG) surgery. We recruited men and women (n=30/sex) with coronary artery disease (CAD) undergoing CABG at the regional St. Mary’s Heart Center (IRB approved). At the time of surgery, blood, PVF and subcutaneous fat (SF) were obtained after consent. PVF size was determined using non invasive 2D Transthoracic Echocardiogram. Gene expression analysis of adipose derived factors in the PVF and SF was determined using quantitative PCR. Circulating levels of inflammatory factors and adipokines were determined using multiplex arrays. PVF size (ECHO) and biochemical parameters were correlated to clinical endpoints obtained from the Society of Thoracic Surgery database. Rank- sum Mann Whitney analysis showed sex differences in PVF size within patients with CAD. A significant correlation was observed between PVF size and BMI. Gene expression of adiponectin (anti-inflammatory) was lower but pro-inflammatory CX3CL1 and CCL22 were higher in the PVF of patients with hypertension compared to normotensives. Our studies provide evidence for PVF derived factors and increased risk to CAD and hypertension.

Cell Signalling Session 1D

CS01 GSK3 phosphorylates the actin regulatory protein CAP1 to control the actin cytoskeleton and cell polarization

Guo-Lei Zhou, Ph.D.
Assistant Professor, Arkansas State University
gzhou@astate.edu

Guo-Lei Zhou, Ph.D., Pooja Gha1,2, Huhehasi Wu1, Haitao Zhang1,2, Jeffrey Field3 & Guo-Lei Zhou1,2 1. Department of Biological Sciences, Arkansas State University, State University, AR 72467 2. Molecular Biosciences Program, Arkansas State University, State University, AR 72467 3. Department of Pharmacology, University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA 19104

Cell signaling has long been recognized to control the actin cytoskeleton and cell motility; the underlying mechanisms, however, remain insufficiently defined. Cyclase-associated Protein 1 (CAP1) is a highly conserved actin sequestering protein that facilitates actin dynamics through both coflin-dependent and -independent mechanisms. We found that mammalian CAP1 is a phospho-protein, and mapped 9 phosphorylation sites in Thr24, Ser25, Ser36, Ser217, Ser227, Ser247, Ser307, Ser309 and Thr314. By expressing mutant proteins, we found that phosphomimetic mutations at Ser36 and Ser309 caused actin cytoskeletal changes in lamellipodia, stress fibers and cell polarity, suggesting that these sites were phosphoregulatory sites. Kinase assays pinpointed Ser309 as a Glycogen Synthase Kinase 3 (GSK3) site, with Thr314 serving as the priming site (motif: SXXXXT). Inhibition of GSK3 in hTERT-HPNE pancreas cells reduced CAP1 phosphorylation, and led to loss of both cell polarity and CAP1 localization to the leading edge, suggesting roles for both CAP1 and its phosphorylation by GSK3 in cell polarization and migration. Using a phospho-specific antibody against Ser307/Ser309, we found that the phosphorylation was reduced in cells undergoing dynamic actin cytoskeletal rearrangement but elevated in cells with a static actin cytoskeleton, suggesting that the phosphorylation likely reduces CAP1 activity. GST-cofilin pull-down assays and actin co-precipitation of a 6xHis-tagged CAP1 with NI-NTA revealed that the S307D/S309D mutant had reduced binding with both coflin and actin. GSK3 plays roles in a variety of cell functions including cell polarization and migration, and our findings suggest that phosphorylation of CAP1 likely mediates some of the relevant GSK3 signals.
CS02  Inhibiting recognition of the B-cell receptor by the tyrosine kinase Syk

Timothy M. Horton
Undergraduate Student, Ouachita Baptist University, Arkansas
hor46650@obu.edu

Timothy M. Horton, Patrick R. Visperas, John Kuriyan Department of Molecular and Cell Biology and Department of Chemistry, California Institute of Quantitative Biosciences and Howard Hughes Medical Institute, University of California, Berkeley, California, USA; Physical Biosciences Division, Lawrence Berkeley National Laboratory, Berkeley, California, USA

The tyrosine kinase Syk (spleen tyrosine kinase) is essential for the proper function of the immune system due to its integral role in B-cell signalling. Stimulation of a B-cell relies on recognition of a foreign antigen by the B-cell receptor. Syk acts as a molecular “on/off” switch, linking B-cell stimulation to B-cell activation. Syk is recruited to ITAMs (Immunoreceptor Tyrosine-based Activation Motifs) on the B-cell receptor by its tandem-SH2 (Src Homology 2) domains. Preventing Syk’s recruitment to the B-cell receptor is one method for curtailing autoimmune diseases such as rheumatoid arthritis. Disruption of ITAM binding to the SH2 domains of Syk was observed in the presence of a small molecule found to inhibit ZAP-70, a functional analogue in T-cells. One cysteine in particular, cysteine 206, was determined necessary for inhibition based on mutation studies. Mass spectrometry confirmed that this cysteine was covalently modified by the inhibitors. A parallel study indicated that H2O2 also acts as an inhibitor of Syk:ITAM binding. Mutation of cysteine 206 protects Syk from inhibition by H2O2. This finding suggests that Syk may be subject to a redox inhibitory feedback mechanism. The analogous role of cysteine 206 in both instances of inhibition suggests that the inhibitory compounds examined may recapitulate this cellular inhibitory mechanism.

CS03  Global phosphoproteomic analyses define host signaling networks usurped for gammaherpesvirus replication

James A. Stahl
Graduate Student, University of Arkansas for Medical Sciences
jastahl@uams.edu

James A. Stahl (1), Shweta S. Chavan (2, 3), Jeffrey M. Sifford (1), Veronica MacLeod (2), Daniel E. Voth (1), Ricky D. Edmondson (2), and J. Craig Forrest (1) (1) Dept. of Microbiology and Immunology and Center for Microbial Pathogenesis and Host Inflammatory Responses, (2) Myeloma Institute for Research and Therapy, and (3) UALR/UAMS Joint Program in Bioinformatics, University of Arkansas for Medical Sciences, Little Rock, AR 72205

Lytic gammaherpesvirus (GHV) replication facilitates the establishment of lifelong latent infection, which places the infected host at risk for numerous cancers. As obligate intracellular parasites, GHVs must control and usurp cellular signaling pathways in order to successfully replicate, disseminate to stable latency reservoirs in the host, and prevent immune-mediated clearance. To facilitate a systems-level understanding of phosphorylation-dependent signaling events directed by GHVs during lytic replication, we utilized label-free quantitative mass spectrometry to interrogate the lytic replication cycle of murine gammaherpesvirus-68 (MHV68). Compared to controls, MHV68 infection regulated by 2-fold or greater ca. 86% of identified phosphopeptides – a regulatory scale not previously observed in phosphoproteomic evaluations of discrete signal-inducing stimuli. Network analyses demonstrated that the infection-associated induction or repression of specific cellular proteins globally altered the flow of information through the host phosphoprotein network, yielding major changes to functional protein clusters and ontologically associated proteins. A series of orthogonal bioinformatics analyses revealed that MAPK and CDK-related signaling events were overrepresented in the infection-associated phosphoproteome and identified 155 host proteins, such as the transcription factor c-Jun, as putative downstream targets. Importantly, functional tests of bioinformatics-based predictions confirmed ERK1/2 and CDK1/2 as kinases that facilitate MHV68 replication and also demonstrated the importance of c-Jun. Finally, a transposon-mutant virus screen identified the MHV68 cyclin D ortholog as a viral protein that contributes to the prominent MAPK/CDK signature of the infection-associated phosphoproteome. Together, these analyses enhance an understanding of how GHVs reorganize and usurp intracellular signaling networks to facilitate infection and replication.
CS04  Productive MHV68 infection compromises the cellular p53 signaling pathway

Jeffrey Sifford
Graduate Student, University of Arkansas for Medical Sciences
JSifford@uams.edu

Jeffrey Sifford, Eduardo Salinas, James A. Stahl, and J. Craig Forrest, Department of Microbiology and Immunology, University of Arkansas for Medical Sciences

While gammaherpesviruses (GHVs) are etiologically associated with many diseases and malignancies, mechanisms by which GHVs block host cell stress responses, particularly those involved in tumor suppression, to efficiently replicate and colonize the host are incompletely defined. Among the critical cellular stress responders is the tumor suppressor protein p53, a key regulator of the cell cycle and cell death. We utilized murine gammaherpesvirus-68 (MHV68), a natural rodent pathogen that provides a tractable small animal model for GHV infection and disease, to dissect GHV interactions with the host tumor suppressor protein p53. MHV68 infection induced robust p53 stabilization in cultured fibroblasts and in splenocytes in vivo. The stabilization and phosphorylation of p53 required early viral gene expression, but not MHV68 DNA replication. Although p53-responsive cellular genes were induced early during infection, their expression subsided as infection progressed, even though p53 remained stable and phosphorylated. Further, infected cells lost responsiveness to p53-activating stimuli as the replication cycle progressed, as p53-inducing chemotherapeutics failed to elicit p53-responsive gene expression. Loss of p53 signaling in response to exogenous stimuli correlated with protection against p53-driven apoptosis. p53 inactivation still occurred in MHV68-infected cells in the absence of late gene expression, implicating an early MHV68 gene in p53 inhibition. Finally, cells infected with an mLANA-null mutant virus remained responsive to p53 agonists and were not protected against p53-mediated cell death. However, mLANA was insufficient to inactivate p53. Collectively, these data suggest that GHV replication elicits p53 activation and stabilization, which is later functionally inactivated by mLANA in concert with other early genes.

CS05  HUWE1 is a molecular link controlling RAF-1 activity supported by the Shoc2 scaffold

Emilia Galperin, Ph.D.
Assistant Professor, University of Kentucky
emilia.galperin@uky.edu

Emilia Galperin, Eun Ryoung Jang, Ping Shi, Myoungkun Jeoung Jamal Bryant Department of Molecular & Cellular Biochemistry University of Kentucky Lexington, KY

The extracellular signal-regulated kinases (ERK1/2) signaling pathway is critical in normal human development as it controls essential cellular processes. When these processes are perturbed, malignant transformations and cardiovascular pathologies can develop. The ERK1/2 pathway transmits signals to diverse biological outcomes. Signaling specificity is delivered by scaffolds that assemble multi-protein complexes, compartmentalize them at particular cellular locations, and regulate accessibility to substrates. Hence, scaffold proteins not only have a huge impact on the biological behavior of the ERK1/2 pathway. Shoc2 is a critical scaffold that accelerates ERK1/2 signaling through tethering Ras and Raf-1 signaling components. Ablation of Shoc2 in mice resulted in early embryonic lethality due to severe heart defects. An N-terminal serine to glycine (S2G) substitution in Shoc2 is found in patients with Noonan-like (NL) syndrome. We found that Shoc2 interacts with a member of the HECT domain-containing family of E3 ubiquitin ligases, a large E3 ligase HUWE1. HUWE1 is implicated in the regulation of cell proliferation, apoptosis, and DNA damage response. Our data demonstrate that HUWE1 is a part of the Shoc-Ras-Raf-1 signaling complex. Depletion of HUWE1 resulted in decreased Shoc2 ubiquitination and increased Shoc2 protein stability. Furthermore, ubiquitination, stability of the Shoc2 signaling partner - Raf-1, and subsequent ERK1/2 activation were also affected by HUWE1 knock-down. Importantly, HUWE1 affected Raf-1 stability and ubiquitination in a unique, Shoc2-dependent manner. Thus, we identified a novel functional interaction between Shoc2 and HUWE1 that plays a role in allosteric regulation of the ERK1/2 signals transmitted through the Shoc2 scaffolding complex. Our data suggests that in the context of the Shoc2 “platform”, HUWE1 recognizes and ubiquitinates Shoc2 and Raf-1 in a spatio-temporally controlled manner, thus affecting kinetics of ERK1/2 activity.
GM01  Luminescent sensing and imaging through tissue

Jeffrey Anker, Ph.D.
Assistant Professor, Clemson University
janker@clemson.edu

Jeffrey Anker, Melissa M. Rogalski, Clemson University Josh Lake, Clemson University John DesJardins, Clemson University

The surface of implanted medical devices is a region with interesting chemical and mechanical processes to monitor. However, there is a lack of medical imaging techniques for surface-specific chemical imaging (e.g. pH) at high resolution through tissue. Although fluorescence-based chemical and mechanical sensors are sensitive and versatile, their utility for in vivo imaging is limited by interference from tissue autofluorescence and by optical scattering which drastically reduces image resolution. To avoid these issues, we are developing “smart implants” coated with X-ray scintillator films that serve as an internal X-ray addressable light sources: The scintillator film generates a luminescent spot when and where it is irradiated by an external X-ray beam. pH indicator dyes in the film modulate the spectrum of the light escaping through the tissue, thus allowing the local pH to be determined spectroscopically. The pH on the implant surface can be mapped point-by-point by scanning the X-ray beam over the scintillator film and collecting the spectrum at each point. We demonstrate submillimeter resolution imaging through tissue, limited by the X-ray beam width. We also observe pH decreases in time due to bacterial growth on the films. This approach has great potential for noninvasively studying chemical and physical processes on implanted medical devices.

GM02  A Novel Bioassay to Identify Chemical Regulators of Stem Cell Self-Renewal

Angus MacNicol, Ph.D.
Professor, University of Arkansas for Medical Sciences
Angus@UAMS.edu

Angus MacNicol, MacNicol, M.C., Center for Translational Neuroscience, University of Arkansas for Medical Sciences, Cragle, C.E., UAMS Penthala, N.R., UAMS Janganati, V., University of Arkansas for Medical Sciences Hardy, L.L., Center for Translational Neuroscience Crooks, P.A., University of Arkansas for Medical Sciences

A subpopulation of cells in solid tumors possess stem cell self-renewal function and are responsible for tumor progression and recurrence. Because few therapeutic strategies are available to target these cells, identification of novel reagents capable of attenuating tumor-initiating cell self-renewal and survival are critically important for development of improved therapies to treat and cure breast cancer. Recent evidence suggests that regulated mRNA translation plays a key role in controlling stem cell growth and survival and is thus an important and underdeveloped therapeutic target for cancer control. Indeed in a variety of cancers, tumor cell self renewal, survival and metastasis are regulated by Musashi-dependent mRNA translational control. Because of concomitant transcriptional regulation, the specific targeting of regulated mRNA translational control in mammalian systems had not been readily accessible for small molecule screening. Indeed, no pharmacological inhibitors of Musashi currently exist. To address this challenge, we developed a novel phenotypic bioassay for Musashi function in oocytes of the frog, Xenopus. Gene transcription is suppressed during Xenopus oocyte maturation, enabling direct evaluation of Musashi function without confounding changes to gene transcriptional programs. We have initiated screening a library of 3000 small chemical compounds for modulators of Musashi function in the Xenopus bioassay. An initial proof of concept analysis of 44 potential anticancer parthenolide derivatives demonstrates feasibility of the approach. Together with analysis of validated and prioritized candidate compounds in mammalian oncosphere and xenograft assays our approach will significantly expedite drug discovery for compounds that attenuate cancer stem cell self renewal for treatment of breast, leukemia, brain, colon and lung cancer where Musashi and regulated mRNA translation mediate disease progression.
GM03  A Radial Diffusion Assay for the Rapid Evaluation of Antimicrobial Peptides

Dustin Walter
Undergraduate Student, Ouachita Baptist University, Arkansas
wal51422@obu.edu

Dustin Walter1*, Yazan Akkam2,3, and David S. McNabb2,3

Ouachita Baptist University, Arkadelphia, AR1, Department of Biological Sciences and the Cell and Molecular Biology Program, University of Arkansas, Fayetteville, AR2,3

Antimicrobial peptides (AMPs) have been a major research focus due to their potential to combat a variety of human pathogens. Our laboratory has identified several novel peptides that display significant antifungal activity. The effectiveness of these peptides in vitro has proven promising; however, it has been shown that physiological concentrations of various salts along with other conditions are inhibitory to the activity. To further explore the inhibitory effects of these salts, a new assay was developed whereby we can observe the effects of various salts on the peptide killing activity. For our studies, we employed several clinical isolates of Candida species to evaluate the killing activity of peptides in the presence of physiologically relevant salts at varying concentrations. By adding the salts individually, we are able to examine the inhibitory effect of each. When compared to other assays, the new assay requires less time and resources by allowing us to test the AMPs under numerous conditions simultaneously. After testing the AMPs, we determined that CaCl2, MgSO4, NaCl, and KCl are all inhibitory to peptide killing activity at varying degrees. In addition, we discovered that circularization or hexanoic acid modification of the peptide bypasses the inhibition of salts. Our long term goal is to modify the peptides in a way that will allow for their use in vivo.

GM04  Surface epitopes of CD2 protein to inhibit CD2-CD58 protein-protein interaction as therapeutic agent for arthritis

Ameya S. Gokhale, Ph.D.
Graduate Student, University of Louisiana at Monroe
gokameya@gmail.com

Ameya S Gokhale, Dr Seetharama Satyanarayanajois, University of Louisiana at Monroe

Many biological processes, including transmembrane signal transduction, cell regulation, and the immune response are regulated through Protein-protein interactions (PPI). Immune signaling, in normal physiology is governed in the form of 2 signals wherein cell adhesion molecules play an important role. CD2 and its ligand CD58 (LFA-3) are the cell adhesion molecules that participate in the early phase of immunological response. In pathology of Rheumatoid Arthritis, CD58 is seen to be upregulated which facilitates further activation of T-lymphocytes and ultimately results into severe arthritis and bone destruction. In our lab, we aim to inhibit this CD2-CD58 PPI by designing peptides from the epitopic portions of CD2 protein. This peptide was designed using (D)-Pro-Pro moiety to induce β-turn to give a stable conformation. The specific aims of the project were: a) to evaluate the cell adhesion inhibition activity of peptide using lymphocyte-epithelial cell adhesion assay and E-rosetting assay, b) to elucidate the three-dimensional structure of the peptide using NMR and Circular dichroism (CD) studies, c) to determine specific binding of peptides to CD58 protein and d) to evaluate the efficacy of peptides in in vivo assay in DBA/1 model of collagen induced arthritis (CIA) mice. Among the various peptides designed and synthesized, peptide 6 exhibited cell adhesion inhibition activity in nanomolar concentration (7 nM) in the in vitro assays. It was also very effective in suppressing CIA in DBA/1 model of mice as seen from arthritis scoring and histopathology analysis. Part of this project was supported by summer research program of Louisiana Biomedical research with the funding from the National Institutes of Health through the National Institute of General Medical Sciences Grant 8P20GM103424.
GM05  Purification of a Specific Native Genomic Locus for Proteomic Analysis

Stephanie Byrum, Ph.D.
Post Doctoral Fellow, Univ of Arkansas for Medical Sciences
sbyrum@uams.edu

Stephanie Byrum, Ph.D., Alan J. Tackett; Univ of Arkansas for Medical Sciences

We describe a novel approach to isolate native chromatin sections without genomic engineering for label-free proteomic identification of associated proteins and histone post-translational modifications. A transcription activator-like (TAL) protein A fusion protein was designed to recognize a unique site in the yeast GAL1 promoter. The TAL-PrA fusion enabled chromatin affinity purification (ChAP) of a small section of native chromatin upstream from the GAL1 locus, permitting mass spectrometric (MS) identification of proteins and histone post-translational modifications regulating galactose-induced transcription. This TAL-ChAP-MS approach allows the biochemical isolation of a specific, native genomic locus for proteomic studies, and will provide for unprecedented objective insight into protein and epigenetic mechanisms regulating site-specific chromosome metabolism. The work presented is supported by the NIH Office of the Director, NIGMS, Arkansas INBRE and COBRE funding.

Infectious Disease/Immunology I Session 2B

ID01  Lipid rafts influence the formation of immunoproteasomes via RIP2/NLR pathway against Klebsiella pneumoniae

Sanjay Batra, Ph.D.
Assistant Professor, Louisiana State University
sbatra@lsu.edu

Sanjay Batra, Ph.D., W. J. Kuhs, X. Li, L. Jin and S. Jeyaseelan  Department of Pathobiological Sciences, LSU, Baton Rouge, LA.

Background and Objective: Lower respiratory tract infections remain the most significant cause of infectious disease morbidity worldwide. Receptor interacting protein (RIP)2 is an adaptor for both Toll-like receptors (TLRs) and NOD-like receptors (NLRs) signaling cascades. Ubiquitination of RIP2 and NLR proteins is critical for RIP2/NLR signaling pathways. We observed that RIP2 and NLR proteins play a key role in regulating innate immune responses against Gram-negative bacteria. However the molecular mechanisms associated with RIP2/NLR protein (NLRP6) mediated immune responses have not been explored in detail. Methods: We used methyl-β-cyclodextrin (MβCD) for lipid rafts disruption and MβCD-cholesterol complex to replenish cholesterol for determining the role of lipid rafts in immunoproteasome formation in response to Klebsiella pneumoniae (Kp) and LPS. Bone marrow-derived macrophages (BMDMs) from WT and RIP2/- mice were used to determine the role of proteasomes in RIP2-NLR pathway and formation of immunoproteasomes during Kp infection. Results: Disruption of lipid rafts or deletion of RIP2 leads to reduced expression of immunoproteasome subunits viz. LMP2, LMP7 and MECL-1 in THP-1 and BMDMs respectively in response to Klebsiella or LPS challenge. Proteasome inhibitors markedly reduced Klebsiella mediated immune responses in BMDMs from C57Bl/6 mice whereas their effect was modest on BMDMs from RIP2/- mice. Immunoproteasome formation was independent of RIP2 tyrosine kinase activity. Discussion and Conclusions: We demonstrate: 1) a novel role of lipid rafts and RIP2 in regulating immunoproteasomes formation in response to K. pneumoniae, and 2) ubiquitination of RIP2 plays important role in regulating innate immune responses against K. pneumoniae. Disclosures: The authors have no financial conflicts of interest. Grant Support: This work was supported by NIH (RO1), ARRA & Scientist Award (FAMRI) to SJ and COBRE, SVM Corp Funding and YCSA from FAMRI to SB.
**ID02**  
**Ibrutinib, a potential treatment for chronic Graft versus Host Disease inhibits T-helper 17 activation and release of IL-17A**

Carrie S. Yang  
Undergraduate Student, Hendrix College  
yangcs@hendrix.edu

Carrie S. Yang, Jason A. Dubovsky, Danielle L. Chappell, Bonnie K Harrington, Samantha Jaglowski, Amy J. Johnson, Natarajan Muthusamy, John C. Byrd  
Ohio State University Comprehensive Cancer Center

Allogeneic hematopoietic stem cell transplant (HSCT) is the only curative treatment for many hematologic cancers. The success of HSCT is underpinned by graft-anti-tumor immunity termed GVT, yet this is severely hampered by the multifactorial autoimmune complications arising from chronic graft versus host disease (cGVHD). Current therapeutics cannot distinguish between cGVHD and GVT and, as a result, are ineffective at combating autoimmunity and can trigger cancer relapse. Ibrutinib represents a first-in-class irreversible ITK/BTK inhibitor with the established capacity to inhibit specific immune subsets integral to cGVHD, including B-cells and Th2 T-cells. Furthermore, GVT-integral Th1 and CD8 T-cells contain an ITK inhibitor-bypass in the form of RLK, thereby preventing inhibition and potentially preserving the GVT effect. Given our understanding of ITK, RLK, and BTK expression in immune cell subsets we hypothesize that in addition to preserving immune-protective T-regulatory cells (Tregs), ibrutinib will block profibrotic and cGVHD-deleterious Th17 T-cells. Our studies confirm that ibrutinib limits human Th17 cell activation and profibrotic IL17a cytokine release after ex-vivo T-cell receptor (TCR) stimulation. Moreover, comprehensive murine in-vivo and human ex-vivo functional analysis revealed that ibrutinib preserves Treg numbers and immune-suppressive function. Our cumulative data along with an impressive clinical safety profile indicate that ibrutinib may represent a targeted therapeutic with the specific capacity to limit cGVHD while preserving GVL after HSCT.

**ID03**  
**Enhancement of Gammaherpesvirus Productive Infection by TRIM21 as Revealed through a Proteomics-based LANA Interaction Screen**

Eduardo Salinas  
Graduate Assistant, University of Arkansas for Medical Sciences  
esalinas@uams.edu

Eduardo Salinas, Stephanie D. Byrum, Linley Moreland, Samuel G. Mackintosh, Alan J. Tackett, J. Craig Forrest

The latency-associated nuclear antigen (LANA) is a conserved, DNA-binding protein encoded by the ORF73 gene in gamma-2-herpesviruses including Kaposi Sarcoma-associated herpesvirus (KSHV) and murine gammaherpesvirus-68 (MHV68). Roles for LANA in latent viral genome replication and maintenance are well known, but LANA proteins also control the efficiency of lytic viral replication and reactivation from latent infection, presumably by regulating host and viral gene expression and host cell death. However, host cell and/or viral proteins that interact with LANA to facilitate viral replication are not yet known. To this end, we have conducted a mass spectrometry-based interaction screen for proteins that engage MHV68 LANA during lytic viral replication using the Isotopic Differentiation of Interactions as Random or Targeted (I-DIRT) differential proteomics technique. I-DIRT employs basic biophysical interaction principles and stable isotopic labeling of amino acids in cell culture as a means to identify specific and nonspecific LANA-binding proteins, thereby enabling a more rapid and effective prioritization and biological screening of candidate interaction partners, although a number of host proteins previously demonstrated to engage LANA during latent KSHV infection scored as “non-specific” interactors. We identified the viral tegument protein ORF52 and the host E3 ubiquitin ligase tripartite motif protein 21 (TRIM21), a protein with multiple roles in cell-intrinsic innate immune responses, as “specific”, previously unidentified interactions. We validated the physical interactions between LANA and ORF52 or TRIM21 by co-immunoprecipitation and in vitro pulldown assays. Importantly, shRNA knockdown experiments demonstrate that TRIM21 positively regulates MHV68 lytic replication. Thus, these experiments provide a novel resource for defining LANA functions in lytic GHV replication.
**ID04**  
**A quantitative evaluation of the binding affinity between antibody decorated liposomes and the antigen using SPR**

Yun Xiang  
Graduate Student, Bioengineering Clemson University  
yxiang@clemson.edu

Yun Xiang, Bioengineering Clemson University. Yun Xiang, Raisa Kiseliva, Alexey Vertegel; Bioengineering Clemson University

Targeting is still one of the biggest problems for drug delivery. Clinical application of many drugs is hinged by our inability to achieve desired drug concentration at the site of action. If drugs were efficiently delivered to their target site, side effects could be considerably decreased while the therapeutic effect could be increased. Nanoparticles and liposomes, can be actively targeted to the desired site using specific binding between biomolecules. Antibody is one of promising active targeting agents because of its high affinity, specificity, and availability of antibodies to a broad range of antigens. Though much research has been done on various antibody-decorated nanocarriers, little quantitative results are available on thermodynamics and affinity. Thus, we used surface plasmon resonance (SPR) to determine effect of the antibody loading on the binding affinity of the antibody-coated liposomes. One secondary antibody (goat anti-mouse IgG) and one primary antibody (anti-muc1 antibody) were used as model antibodies, and the antigens were primary antibodies built in mouse and muc1 fiber, respectively. Results from SPR studies confirmed high affinity of liposomes decorated by antibody for their antigens. (KD was in the range of 10-10 ~ 10-11 M). Binding affinity was found to initially increase with the increase of the antibody/liposome ratio, followed by saturation of the affinity constant upon reaching a threshold loading (5-6 antibody/liposome ratio). Further increase of the antibody/liposome ratio did not lead to a significant change in the binding affinity of the liposomes. Also, SPR studies also revealed that, with similar antibody/liposome ratio, larger liposomes had higher binding affinity, indicating that at otherwise similar conditions larger liposomes could provide better targeting. These results are crucial for the preparation of pharmaceutical antibody coated nanocarriers, to prepare cost efficient formulations with maximized binding ability.

**ID05**  
**Characterization of the nitrogen regulatory protein AREA in the dimorphic fungus Histoplasma capsulatum**

Logan Blancett  
Graduate Student, The University of Southern Mississippi  
logan.blancett@usm.edu

Logan Blancett, Thomas Buford & Glen Shearer Same Institution as Presenting Author

Histoplasma capsulatum (Hc) is the etiological agent of histoplasmosis, a common cause of respiratory mycoses in humans. Hc is a dimorphic organism existing as a multicellular mold (M) in soil (or when grown in the laboratory at 25°C) and once inhaled by host (37°C) undergoes a dimorphic shift to the yeast (Y) phase. This dimorphic shift is essential for the pathogenesis of the organism within the host. It is most commonly found in the United States along the lower Mississippi and Ohio River Valley regions where the soil is enriched with nitrogen from high levels of bird and bat excrements. In most fungi repression of complex nitrogen source utilization genes is seen when a favored nitrogen source is present, such as glutamine or ammonia. This phenomenon is called nitrogen catabolite repression (NCR). NCR has been extensively studied in the bakers yeast S. cerevisiae as well as the filamentous fungi Aspergillus spp. and N. crassa. AreA has been characterized as the key negative-regulator of NCR in filamentous fungi. AreA represses transcription pathways of less energetically favored nitrogen sources in the presence of preferential nitrogen sources. AreA contains three highly conserved domains across fungal species: an N-terminus, DUF 1752 and a GATA zinc finger. An AreA homolog has been identified in Hc that contains all three domains. The focus of this study is to begin experimentally determining if the AreA homolog found is the key negative regulator of nitrogen metabolism in Hc. RT-PCR shows that AreA is down-regulated when subjected to nitrogen starvation conditions. This down-regulation is consistent with AreA being involved in NCR. Current work is underway to over-express the gene as well as RNA interference to characterize AreA. This work was supported by the Mississippi INBRE, funded by an Institutional Development Award (IDeA) from the National Institute of General Medical Sciences of the National Institutes of Health under grant number P20GM103476.
NS01  Control of neural stem cell differentiation and survival through manipulation of Musashi-mediated mRNA translation

Melanie C. MacNicol, Ph.D.
Assistant Research Professor, Center for Translational Neuroscience, University of Arkansas for Medical Science
macnicolmelanie@UAMS.edu

Melanie C. MacNicol, Ph.D., Center for Translational Neuroscience, University of Arkansas for Medical Science, Angus M. MacNciol, Ph.D., Winthrop P. Rockefeller Cancer Inst., University of Arkansas for Medical Science

Stem cell therapy shows unique promise for aiding recovery from neurological damage. Currently, reliable treatment with therapeutic stem cells is hampered by lack of control of stem cell self-renewal, differentiation and survival. Recent studies have suggested that mRNA-processing mechanisms play a pivotal role in stem cell biology however, our lack of understanding of mRNA control mechanisms limits our use of these mechanisms to control stem cells. In this study, we demonstrate that manipulation of the function of the mRNA control protein, Musashi, specifically promote self-renewal and survival of primary neural stem/progenitor cells in vitro. We examine the mechanisms mediating these biological responses. Our findings suggest that RNA-control mechanisms may present a therapeutic target to aid progress towards use of stem cells in neurological regenerative therapies.

NS02  Nrf2 Activation as Novel Therapeutic Strategy for ALS and its Neuroprotective Mechanisms in Astrocytes and Motor Neurons

Mahmoud Kiaei, Ph.D.
Assistant Professor, University of Arkansas for Medical Sciences
mkiaei@uams.edu

Mahmoud Kiaei, Ph.D., Shilpi Yadav., Mohammad A. Esmaeili, #Michael B., Sporn, #Karen T., Liby, and §M. Flint Beal.
Department of Neurobiology and Developmental Sciences, Center for Translational Neuroscience, University of Arkansas for Medical Sciences, Little Rock, AR, USA, #Department of Pharmacology, Dartmouth Medical School, Hanover, NH 03755, USA, § Department of Neurology and Neuroscience, Weill Medical College of Cornell University, New York, NY, USA.

Amyotrophic lateral sclerosis (ALS) is a fatal neuromuscular disease with no cure. We have identified Nrf2 (nuclear factor-erythroid-2-related factor-2) as a novel and promising target that can potentially block at least 3 major toxic pathways. Nrf2 is a transcription factor, and regulate the expression of Phase II genes in all cell types to exert protective reaction(s) against toxicity and insults. We have shown that two synthetic triterpenoids (CDDO-ethyl amide (EA) and CDDO–trifluoroethyl amide (TFEA)) that potently activate Nrf2, are efficacious in an ALS mice model (SOD1G93A mice), and significantly extend lifespan (Neymotin et al., 2011). We assayed Nrf2 nuclear translocation, mitochondria function, cytochrome c release, and cell viability in mouse primary motor neurons and astrocytes. We will present further evidence of Nrf2 target validation by using triterpenoids as a tool and novel drug, to unravel the mechanisms of Nrf2/ARE neuroprotection. We present our findings on the effect of Nrf2 activation in improving mitochondrial function and preventing cytochrome c release in human and mouse ALS primary astrocytes and motor neurons. Our data suggest that Nrf2 is a neuroprotective target that its activation blocks multiple toxic pathways in ALS and drugs that regulate Nrf2/ARE signaling pathway (e.g. triterpenoid CDDOs) are of great interest. Further studies are warranted to evaluate the in vitro and in vivo effect of Nrf2 activation and fully unravel its neuroprotective mechanisms to pave the way for the development of Nrf2 based therapy that may significantly alter disease course in patients suffering from ALS. Acknowledgements: Authors acknowledge the support by grants from NIH-NINDS to MK, University of Arkansas for Medical Sciences startup fund, and University of Arkansas for Medical Sciences center for translational Neurosciences. Also, authors acknowledge the support by grants from the National Center for Research Resources (SP20RR020146-09) and the National Institute of General Medical Sciences (8 P20 GM103425-09).
NS03  Calpain Inhibition Blocks Tributyltin Induced Neurodegeneration

Miki S. Lindsey
Undergraduate Student, University of Central Arkansas
bvohra@uca.edu

Miki S Lindsey, Bhupinder P. S. Vohra, Biology Department, University of Central Arkansas, Conway

Tributyltin (TBT), an endocrine-disrupting chemical, has been used as a heat stabilizer, an agricultural pesticide, and a component of antifouling paints. When TBT degrades it produces dibutylin and monobutylin which are toxic to diverse organisms, including humans. In the present study we found that TBT exposure lead to extensive axonal and neuronal cell body degeneration in the in vitro cultured dorsal root ganglion neuron. We discovered that TBT upregualtes neuronal calcium levels which is followed by the activation of calpains. Inhibition of apoptotic pathways by overexpression of Bcl-xl did not block neuronal demise in TBT treated neurons, and overexpression of Nmnat1 also failed to provide axonal protection in these conditions. However, overexpression of calpastatin in these neurons inhibited the TBT induced calpain activation and neuronal death. Thus we conclude that mitochondrial apoptotic pathways or Nmnat mediated pathways do not play a significant role in TBT neurotoxicity and the calpain inhibitors can be utilized as a potential protective agent in TBT induced neurodegeneration.

NS04  Utilizing the ensemble docking method for ranking and selection of representative cannabinoid receptor subtype 2 (CB2) models

Pankaj Pandey
Graduate Student, The University of Mississippi
ppandey@go.olemiss.edu

Pankaj Pandey, Kuldeep K. Roy, Ronak Y. Patel, Robert J. Doerksen* Department of Medicinal Chemistry, School of Pharmacy, University of Mississippi, University, MS, USA 38677

The cannabinoid receptor subtypes 1 and 2 (CB1 and CB2) belong to class A, G-protein coupled receptors, and represent therapeutically important targets for neuropathic, inflammatory, glaucoma, and neuro-degenerative disorders. Despite the considerable advancement of X-ray/NMR techniques, there is no available experimental structure of CB receptors. Hence, theoretical CB structures predicted using homology techniques, are being utilized to facilitate CB drug discovery. Furthermore, the fact that multiple receptor conformations are possible for any target represents a big challenge for structure-based drug design or virtual screening. In such a challenging scenario, ensemble docking is a useful method to identify some representative conformations of any target. Herein, we report the identification of some representative CB2 receptor conformations utilizing the ensemble docking method. We developed 150 CB2 models using the Modeler software based on bovine rhodopsin (PDB-Id: 1F88) as template. Quality assessment was done using the Procheck program which suggested a total of 132 good quality CB2 models. The ensemble docking of resveratrol analogues into these 132 CB2 models ranked a total of six models that explained well the observed structure-activity relationship (SAR). Further assessment of these six models through docking of four representative CB2 agonists suggested only three of the CB2 models capable of explaining well the binding modes of the considered agonists. Comparative analysis suggested the particular importance of the orientations mainly of two residues Ser28(7.39) and Lys109(3.28) in each of the best three CB2 models for agonist binding. The orientations of these residues were different in the other three models, leading to their failure to explain the agonist binding modes. Therefore, the identified three best models represent three different CB2 receptor conformations and may further be utilized for the identification of new potential CB2 ligand(s).
Cytokines are proteins that are emitted by cells in the immune system to carry out various communication functions. These proteins are of significant biomedical interest because of their role in inflammation related to many disease states. For this reason, there has been an increased interest in the applications of microdialysis sampling of cytokines. Microdialysis sampling is a minimally-invasive in vivo sampling method that has been used in neuroscience applications for more than 30 years. For animal studies, the devices are typically 500 µm or less (outer diameter) and 4-10 mm in length. Microdialysis sampling has also been performed in humans. This technique has been widely used for neurotransmitter collection as well as pharmacokinetic studies for different drugs. Our research group has been interested in the role that macrophages play during the foreign body reaction to implanted biomaterials or devices. For the past ten years, our major research focus has been to use a microdialysis sampling probe as a glucose sensor “mimic” in rat subcutaneous tissue. In these studies, we have measured different cytokines at different time points following probe implantation. Additionally, different cellular modulators (drugs or other cytokines) can be concomitantly infused through the microdialysis sampling implant and monitor localized tissue biochemistry using appropriate chemical analysis tools. For the past two years, our group has successfully performed cytokine collection from rodent brain. We are embarking on using this successful work to monitor the role of cytokines in epilepsy and stroke animal models. Microdialysis sampling has become an exquisite tool to monitor tissue biochemistry that has many applications in biomedicine. This work has been supported by NIH R01 EB 001441, R01 EB-014404 and R21 NS075874.
Jennifer Greene
General Biomedical Sciences, School of Pharmacy, University of Charleston, WV
jennifergreene@go.ucwv.edu

Jennifer Greene, A. Almeida‡, U.K. Reddy‡, and G. Kaushal†* †School of Pharmacy, University of Charleston, Charleston, WV
*Jefferson School of Pharmacy, Thomas Jefferson University, Philadelphia, PA ‡Gus R. Douglass Institute and Department of Biology, West Virginia State University, Institute, WV

Purpose  Our objective is to develop value added pepper varieties adapted to local conditions and extract this natural capsaicin from these peppers to formulate a transdermal gel for chronic back pain. Methods  An HPLC method was developed that could quantify between the two major components of capsaicinoids: capsaicin and dihydrocapsaicin. Eighty-eight Capsicum annuum cultivars were grown and fruits were collected 30 days after pollination. Peppers were chopped and oven dried at 55°C and grounded to a powder. Capsaicin was extracted according to the standard procedure and the samples were further process by solid phase extraction (SPE). For the transdermal patch development, natural capsaicin (80mg) with 1.0mL of ethanol was dissolved in polymeric gels. The gels used were made from the polymers; hydroxypropyl methyl cellulose (HPMC), hydroxypropyl cellulose (HPC), methyl cellulose (MC), and Pluronic F-127 (15%). The release of capsaicin was studied using Distek dissolution apparatus with a modified method of dissolution. Franz diffusion cell was used to determine the in vitro skin permeation of capsaicin. Results  The pepper Cajun tobasco reported the highest amount of capsaicin in the accessions tested of 10.84 mg/gr of total capsaicinoids, followed by the ornamental Bolivian rainbow: 7.02 mg/gr of total capsaicinoids. For the initial characterization for capsaicin patch development, the relationship between the type of gel and elapsed time was plotted. It was noticed that MC gel released the greatest amount of capsaicin in a shorter period of time followed by HPC, HPMC, and then Pluronic F-127. HPLC analysis of the Franz diffusion cell revealed no permeation through the rat skin when using the MC and HPC. Conclusion  The results of this study suggest that further research is needed for more polymer gels, including greater concentrations of current polymer gels, regarding the development of a patch for the transdermal delivery of capsaicin.

Franshawn Mack
Cancer, South Carolina State University
franshawn94@yahoo.com

Franshawn Mack, Dr. Marvella Ford Ms. Dana Burshell Mr. Wei Wei Dr. Elizabeth Garrett-Mayer Medical University of South Carolina

Background: African-Americans (AAs) are disproportionately affected by cancer mortality compared to their European American (EAs) counterparts. While greater participation in cancer clinical trials among AAs could help reduce this disparity, negative trial perceptions could negatively impact trial participation. Objective: To evaluate the reliability of the Attitudes towards Randomized Trial Questionnaire (ARTQ) in assessing perceptions of cancer clinical in predominantly African American populations in South Carolina. Methods: Principal Component Analysis and Cronbach’s alpha estimates were used to assess the reliability of the ARTQ in a convenience sample of 315 participants (81.4% AA), from 2008 to 2013, who lived in South Carolina counties with high racial disparities in cancer mortality rates. Results: Slightly more than half of the participants had at least a college diploma (60.8%), 84.8 % were female, and 53.4 % had an annual income of $40,000+. In this study, Cronbach’s alpha was shown to be 0.86. Conclusion: The ARTQ displayed strong evidence of high statistical reliability. This analysis has great implications for future research because it represents the first test of reliability of the ARTQ in a predominantly African American sample and lays the groundwork for use of the ARTQ in future studies in diverse populations.
NS06  Time-course of effects of growth hormone (GH) and GH antagonist on auditory hair cell regeneration in zebrafish (Danio rerio)

Amy Ni
Neuroscience, Western Kentucky University
michael.smith1@wku.edu

Amy Ni, Mackenzie Perkins, Michael E. Smith Department of Biology, Western Kentucky University, Bowling Green, KY 42101

A previous microarray study found that growth hormone (GH) was significantly upregulated in the zebrafish (Danio rerio) inner ear following sound exposure (Schuck et al. 2011). In subsequent experiments, groups of zebrafish were exposed to a 150 Hz tone at 179 dB re 1 µPa RMS for 36 hours and then given an intraperitoneal injection of either carp GH or buffer. These studies showed that intraperitoneal injection of GH into zebrafish post-acoustic trauma, led to an increase in cell proliferation (BrdU-labeled cells), a decrease in cell death (TUNEL-labeled cells), and increased hair cell density compared to buffer-injected controls (Sun et al. 2011). The purpose of this study was to examine whether the effects of endogenous GH can be blocked with a GH antagonist, and whether exogenous GH injection prior to sound exposure has a prophylactic effect that may mitigate the effects of acoustic trauma on auditory hair cells. Groups of zebrafish were injected with either GH, GH antagonist, or buffer. Immediately following the injection, auditory hair cell damage was induced through exposure to acoustic overstimulation (150 Hz at 179 dB re 1 µPa). Hearing tests were performed on the fish at 0 – 5 days post-trauma via auditory evoked potential (AEP) recordings. Following AEP, fish ears were dissected and fixed overnight in 4% paraformaldehyde. Dissected zebrafish saccules were then subjected to fluorescein-conjugated phalloidin staining and visualized under fluorescence microscopy. GH injection pre-sound exposure improved hair cell density and promoted functional recovery of hearing, with GH-injected fishes exhibiting greater hair cell densities and lower hearing thresholds than buffer-injected controls. While GH has a positive effect on hair cell regeneration and hearing recovery, our results show that GH antagonist has the opposite effect. Whether GH is effective at preventing hair cell loss or promoting hair cell regeneration in mammals is yet to be determined.

ID24  Understanding the mucus production of a human respiratory paramyxovirus infection

Boyang Piao
Infectious Disease/Immunology, Louisiana State University
bpiao1@tigers.lsu.edu

Boyang Piao, MR. Banos-Lara. Louisiana State University M.Antonieta Guerrero-Plata. Louisiana State University

As one of the most clinically relevant respiratory virus in the hospitalization of young children, elderly, and immunocompromized patients, human metapneumovirus (hMPV) is a negative, single strand RNA virus that contains 9 proteins including three surface proteins: glycoprotein (G), fusion protein (F), and small hydrophobic protein (SH). The G protein is responsible for the virus attachment to cell receptors of the host cell, and it has been deemed as a potential vaccine candidate. hMPV mainly infects the upper and lower respiratory tract, replicating primarily in lung epithelial cells. Lung epithelial cells produce mucus which is consisted of mucins. Muc1, Muc 5ac and Muc 5b make up more than 90% of the mucus. However, little is known about their induction in response to hMPV infection. The primary objective of this work is to characterize the production of mucins during hMPV infection in vitro and in vivo and define the role of surface proteins in the production of mucus and mucins. Our results in vitro show that all three mucins have shown an increased expression at the protein and mRNA level, and that is directly proportional to the multiplicity of infection (MOI) and time of infection used. We have also observed that the production of mucins during an hMPV infection is dependent on viral replication. These critical findings have opened up the possibility of determining the role of Muc 1, Muc 5ac, and Muc 5b in hMPV infection in vivo by studying the mechanism(s) that regulate the production of mucins. Understanding the mechanisms of induction of mucins will be a relevant contribution in the design of a potential vaccine candidate for hMPV infection.
**Bioutica II Session 3A**

**BI06 NeedleAnalyzer: A Data Analysis Tool for LCMS-Based Untargeted Metabolomics Data**

C. Stephen Embry  
Graduate Student, University of Arkansas at Little Rock & University of Arkansas for Medical Sciences  
csembry@ualr.edu

**C. Stephen Embry, Dr. Stephen C. Grace(UALR Biology), Heng Luo(UALR/UAMS Bioinformatics)**

There is growing interest in untargeted metabolomics in life and health sciences to identify certain conditions or phenotypes. LCMS is the most common analytical platform in metabolomics research since it provides the broadest coverage of the metabolome and requires relatively simple sample preparation. However, mining LCMS for important features presents a major bottleneck to metabolomics research. Here we introduce a novel platform called NeedleAnalyzer to filter and extract significant features from LCMS, specifically untargeted metabolomic datasets rapidly and efficiently. NeedleAnalyzer is a web server application being developed that can streamline the analysis of metabolomic data from full scan LCMS-based chromatograms output cdf files. The core function of NeedleAnalyzer is to produce a graphical representation of a dataset akin to a “barcode” consisting of all masses parsed into user-defined bins that can be analyzed by exploratory methods such as PCA. Users can also search for target masses and obtain extracted ion chromatograms listing time and intensity values for mass ranges of interest. Graphical visualization of the bin analysis is provided along with traditional forms of data visualizations for mass spectrometry data, total ion chromatograph(TIC), base peak chromatograph(BPC), extracted ion chromatographs(EIC) and mass spectrum. Graphical representation of the outputs can be downloaded, along with comma separated files of all outputs produced, so that the user can export the results to other software for further analysis or customized graphing. A major advantage of NeedleAnalyzer over other LCMS processing platforms is that it provides an unbiased representation of the data since peaks are not assigned to specific masses by retention time indices.

**BI07 nDh-PDPA: n-Dimensional Hybrid Probability Density Profile Analysis**

Arjang Fahim  
Graduate Student, University of South Carolina  
fahim@email.sc.edu

**Arjang Fahim, Homayoun Valafar**

The characterization of a protein using NMR method is expensive and time consuming. In spite of many successful efforts to develop new and economical methods to study novel proteins, characterization of routine proteins remain costly. Probability Density Profile Analysis (PDPA) and the latest version of the software (2D-PDPA) have been successful in identifying the structural homologue of an unknown protein within a library of ~1000 decoy structures. 2D-PDPA utilizes RDC data from one vector type (usually backbone N-H) in two alignment media. PDPA operates by comparing a computed PDP (cPDP) to an experimentally determined pattern of data distribution (ePDP). This comparison has been conducted in an equally spaced grid mechanism between the two PDPs. In order to further expand the selectivity and sensitivity of PDPA, incorporation of additional data is necessary. However, current PDPA approach is limited by its computational requirements, and its expansion to include additional data will render it computationally infeasible. Acquisition of RDC data in additional alignment media is oftentimes straightforward once RDC data are successfully obtained in one alignment medium. However the addition of hybrid data (RDCs, rCSAs, PRE, PCS data) introduces new challenges such as exhaustive search for calculating n-independent order tensors that require an exhaustive search of all possible orientations order tensors. Expansion of these two patterns into n-dimensions will require an exponentially increasing number of comparisons, which also becomes a limiting factor for n > 2. In this report we will introduce n-Dimensional Hybrid Probability Density Profile Analysis (nDh-PDPA) that incorporates nD-RDC analysis, modified comparison technique, and inclusion of high-dimensional, hybrid data. The new approach exhibits tolerable increase in the computation time as a function of increased data, and improves selectivity of structures to within 1.5Å of the actual structure.
BI08    Defining the Recognition Elements of Lewis Y-Reactive Antibodies

Somdutta Saha
Graduate Student, University of Arkansas for Medical Sciences & University of Arkansas at Little Rock
ssaha@uams.edu

Somdutta Saha, Anastas Pashov - 3Stephan Angelov Institute of Microbiology, Bulgarian Academy of Sciences, Sofia, Bulgaria.
Eric R Siegel - 4Winthrop P. Rockefeller Cancer Institute, University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA,
Ramachandran Murali- Department of Biological Sciences, Cedars-Sinai Medical Center, Los Angeles, CA. Thomas Kieber-Emmons - Winthrop P. Rockefeller Cancer Institute, University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA.

Somatic mutations in immunoglobulin genes are perceived to lead to higher affinity antibodies for a specific antigen. The antibody response to carbohydrate antigens in particular are interesting because of the general T-cell-independent nature of the response, suggesting that Variable (V) genes are selected to encode parts of binding sites for components of carbohydrate antigens. Germ-line genes that define carbohydrate-reactive antibodies should therefore sculpt antibody-combining sites containing innate, key side-chain contacts that define the antigen recognition step. To further examine this hypothesis, we analyzed antibodies reactive with the neolactoseries antigen Lewis Y (LeY) to define the residue subset required for the reactive repertoire for the LeY antigen. Our molecular simulation studies of crystallographically determined and modeled antibody-LeY complexes suggests that the heavy-chain germ-line gene VH7183.a13.20 and the light-chain Vκ cr1 germ-line gene are sufficient to account for the recognition of the trisaccharide-H determinant Types 1-4, while the specificity for LeY is driven by the CDR3 backbone conformation of the heavy chain that was shared among the anti-LeY antibodies examined. These results indicate that the monoclonals can “inherit” germ-line-encoded amino acids that are sufficient to recognize trisaccharide-H determinants. Somatic mutations in the periphery of the combining site modify binding affinity for LeY through electrostatic interactions, suggesting that specificity is modulated to some degree by these latter interactions. These observations bring further attention to the separation of recognition from specificity for antigen interactions.

BI09    Investigation of the Mechanism of Apparent HPLC Solvent Interference with an Avidin-Binding Assay

Katelyn Robillard
Undergraduate Student, Southeastern Louisiana University
katelyn.robillard@selu.edu

Katelyn Robillard, Anna Bogusiewicz, Nell Matthews, and Donald Mock; Department of Biochemistry and Molecular Biology, University of Arkansas for Medical Sciences

Biotin, also known as vitamin B7, is an essential coenzyme involved in human metabolic reactions. In studying vitamin deficiencies in newborns, pregnant women, and other adults, a variety of techniques are employed to quantitate biotin and biotin metabolites in biological samples. One of these techniques involves HPLC separation of the metabolites followed by an avidin-binding assay. In recent months, we have observed apparent contamination in the baseline HPLC fractions; these contaminants interfere with quantitation of biotin and biotin metabolites. Both mobile phases of the HPLC gradient exhibit the interference, and both use trifluoroacetic acid (TFA) as the buffer. We hypothesized that the contamination arises from a degradation product of TFA that has avidin-binding characteristics and could be removed by avidin dialysis. Avidin is a tetrameric protein found in the white of chicken eggs. Each avidin molecule forms tight, non-covalent bonds with four molecules of biotin. Our initial study compared the amount of TFA contamination before and after avidin dialysis. Contamination increased after treatment, which is inconsistent with our hypothesis that the contamination should be removed by avidin. Next, we assessed the avidin-binding capacity of avidin in TFA solution (pH 2.2) and compared that to biotin-binding capacity of avidin in water (pH 7.0). Based on assessing the binding of [3H]biotin by dialysis, avidin bound biotin less effectively in TFA than water. Interpretation: The low pH environment of TFA caused denaturation of avidin (unfolding of quaternary and tertiary structures). Conclusion: Avidin is unsuitable for removing the contamination in TFA. In the future, we plan to design a method for removing this contaminant, to define the timing needed for removal, and to investigate conditions that minimize the contamination (e.g., reduce the concentration of TFA).
BI10  XLM: X-linked Peptide Mapping Algorithm

Mihir Jaiswal
Graduate Student, University of Arkansas at Little Rock & University of Arkansas for Medical Sciences
msjaiswal@ualr.edu

Mihir Jaiswal, Nathan Crabtree (UALR/ UAMS joint bioinformatics graduate program, University of Arkansas at Little Rock)
Roger Hall (Division of biomedical informatics, University of Arkansas for Medical Sciences) Boris Zybaylov (Department of bioinformatics and molecular biology, University of Arkansas for Medical Sciences)

Mass spectrometry is a promising tool for protein-protein interaction analysis using chemical cross-linking. A better algorithm was needed for data analysis, to include functionalities for longer sequences, file formats other than .pkl, more than two sequences, semi-specific and non-specific cross-linkers, forced missed cleavage, tandem MS data and O18 radio-labeled peptide spectra. The XLPM algorithm is designed in Perl and MySQL to incorporate above mentioned additional functionalities. The new algorithm takes into account amino acid sequences of proteins, digesting enzyme, chemical cross-linker and missed cleavage level for analysis. In addition, XLPM can handle any number of static as well as variable modifications. It is considerably faster. It identifies cross-linking sites, performs in-silico digestion, calculates the mass values of each combination of fragments with cross-linker, filters them, and matches theoretical masses with experimental masses to identify cross-linked peptides. It also matches tandem MS fragmentation profile to find correct cross-linked species associated with corresponding precursor mass peak. XLPM can identify cross-linked peptide from mass spectrometry data fast and efficiently based on hypothesis, “Detection of a particular b ion with the charge less than that of a precursor implies high probability of detection of the complementary y-ion with remaining charge”. Thus, XLPM has an application in protein-protein interaction studies. XLPM will be made available as a free online tool as well as standalone tool.

BI11  Adapting a computational evolution system to the analysis of RNA-Seq treatment/response differential gene expression data

Nathan Crabtree
Graduate Student, University of Arkansas Little Rock and University of Arkansas for Medical Sciences
nmcrabtree@ualr.edu

Nathan Crabtree, John Bowyer, National Center for Toxicological Research; Jason H. Moore, Dartmouth College

For my dissertation project, I will be modifying a computational evolution system (CES) developed by Dr. Jason H. Moore. This CES will be modified to accept RNA-Seq count/gene data as input. The data will be obtained from peripheral blood sampled from 70 rats split into three treatment groups: control, environment induced hyperthermic (EIH), and neurotoxic amphetamine. The goal of this work is to identify important gene expression changes due to the neurotoxic and hyperthermic effects of amphetamines. CES is a system that uses genetic programming to automatically evolve models of any form (linear/non-linear) that fit the data. CES will choose the smallest subset of genes that can be used to accurately classify and predict the group membership of each sample. CES will narrow down the search space to identify genes with a significant main effect as well as genes with primarily interactive effects on the treatment responses. The results of the CES will be compared to results obtained from RNA-Seq differential expression software. We hypothesize that pathway analyses performed on the gene set identified by CES will be more relevant than pathway analyses performed on all genes identified as significantly differentially expressed. Supported by grants from NCRR (5P20RR016460-11) and NIGMS (8 P20 GM103429-11) at NIH.
CN06  Miniaturized Bioprinting Platform for Personalized Cancer Therapy

Jorge I. Rodriguez-Dévora, Ph.D.
Post Doctoral Fellow, Clemson University
jorger@clemson.edu

Jorge I. Rodriguez-Dévora, Ph.D., Delphine Dean

Medicine has started a rapid developing race toward personalized therapies, promising more effective outcomes and minimizing side effects. In line with this pathway, extrusion based robotic systems can alleviate the task of combining potential chemotherapeutic drugs along biopsied cancerous cells from patients to better predict effect of prescribed treatment. However, up to date these robotic systems have a restricted speed and working volume. Inkjet bioprinting offers capabilities for expediting and downsizing the amount of reagent in such combinatorial analysis. Initial studies using a modified deskjet printer prove to reliably create isolated assays at ranges of hundreds of picoliter at a rate of 213 dots/sec. Consequently, this miniaturized platform was used to evaluate the inhibitory effects of chemotherapeutic drugs over cancerous (HEPG2) and non-cancerous (epithelial) cells seeded in two dimensions. Inhibitory effects were evaluated based on the dose-response curve resulting in half maximal inhibitory concentrations (IC50) of 9.35 and 4.3 mM under cytoxan and DCA treatment, respectively. In comparison to literature, IC50 results are generally in the range of 4-10 mM when using these drugs. Thus our results are consistent with those that used much larger volumes, validating our hypothesis that screening assays can be further miniaturized. Inkjet technology shows promise to be used to determine dosages and treatment modalities using the patient’s limited supply of biopsied cells. Further work will continue toward the fabrication of three-dimensional functionalized microtissues which better mimic the behavior of targeted tissues in vivo, the inclusion of actual cells obtain from patient’s biopsy, and development of automated machine vision and bioinformatics algorithmic approaches to assist in high-throughput rapid screening.

CN07  Monitoring changes in cervical lymph nodes by high-frequency ultrasound in a 4-NQO mouse model of oral cancer

Scott A. Weed, Ph.D.
Associate Professor, West Virginia University
scweed@hsc.wvu.edu

Scott A. Weed, Ph.D., Elyse L. Walk Sarah McLaughlin James Coad All Affiliated with West Virginia University

The most common route of head and neck squamous cell carcinomas (HNSCC) dissemination is via the cervical lymph nodes, making detection of lymph node involvement essential in determining patient prognosis. Evaluation of cervical lymph nodes by clinical ultrasound has been used as a non-invasive procedure to aid in diagnosing nodal status, and when combined with fine-needle aspiration cytology, provides a sensitive and comprehensive means to assess locoregional lymph node metastasis. The development of high-frequency ultrasound (HFUS) technology has provided cancer researchers with a tool for real-time monitoring of tumor formation within animal models in vivo. HFUS has the ability to image structures down to 30 microns, which is useful for 2D in situ measurements of soft tissue structures and to calculate highly accurate tumor volumes. While there are many studies describing the usefulness of HFUS in mouse tumor biology, details regarding the utility of this procedure for studying alterations of cervical lymph nodes in murine HNSCC models are lacking. Here we show that HFUS is capable of monitoring changes in cervical lymph nodes in mice exposed to the oral cancer inducing carcinogen 4-nitroquinoline-1-oxide (4-NQO). Gray scale, power Doppler and contrast-enhanced sonography reveal changes in lymph node size and vascularity following long-term (eight week) exposure to 4-NQO, suggesting that 4-NQO induces early intranodal inflammatory responses. Additionally, we demonstrate that HFUS can be used to perform image-guided fine-needle biopsies on mice with enlarged lymph nodes. We also show that 4-NQO induces HNSCC lymph node metastasis, and that invasive depth of tumor cell penetration into the tongue positively correlates with increased lymph node volume. In summary, this technique is useful for the non-invasive study of oral cancer metastasis in live mouse models and can additionally be applied to the study of diseases that result in cervical lymphadenopathy.
Creating Model Systems to Study the Effects of Ajulemic Acid on Solid Pediatric Tumors

Laura Strossner
Undergraduate Student, Ouachita Baptist University, Arkansas
str49538@obu.edu

Laura Strossner, Amy Eubanks, Joseph Levy, Nathan Koonce, Rob Griffin, Lori Hensley

Ewing’s sarcoma is a highly aggressive primary tumor of the bone most commonly found in adolescent patients in the long bones of the arms and legs. With a low 5-year survival rate of 30%, there is much need for advanced treatment options. Ajulemic acid (AJA) is a non-psychoactive cannabinoid that has become an emerging candidate for a therapeutic agent in solid pediatric cancers. This drug has been found to decrease cell viability and metastatic potential in vitro. While the focus of our lab uses Ewing’s sarcoma as a model system, we have preliminary data with retinoblastoma tumor cells as well. Retinoblastoma is a tumor of the specialized light-sensitive retina in the eye. Up to 95% of patients with this cancer will have success with treatment; however, current treatments leave most patients with vision loss, suggesting benefit from alternative treatments. Our current studies include creating a 3D tumor model, known as a spheroid, to produce a better in vitro model for retinoblastoma tumors. Weri-RB cells will be grown in suspended drops of growth media with endothelial cells and fibroblasts to mimic tumor composition. We can then treat these spheroids with AJA and measure important mediators of tumorigenesis such as VEGF and matrix metalloproteinases in an effort to understand the mechanism our drug is using to produce the observed effects. Ewing’s sarcoma cells have been used in a novel bioluminescent mouse model to demonstrate the drug’s efficacy in vivo. This summer we are creating a metastatic mouse model using Ewing’s sarcoma cells that have been taken from a metastatic lung tumor. It is our hope that these cells injected into the tibiae of the mice will show metastasis to the lungs and that treatment with AJA will decrease the incidence of spread.

Profiling Multiple Myeloma Engraftment Phenomena via an in-vivo SCID Mouse Model and RNA-seq

Shweta Chavan, Ph.D.
Post Doctoral Fellow, University of Arkansas for Medical Sciences
djjohann@uams.edu

Shweta Chavan, Ph.D., Michael Bauer1, Erich Peterson1, Christoph Heuck1, Shmuel Yaccoby1, Donald J. Johann, Jr1. 1Myeloma Institute for Research and Therapy, University of Arkansas for Medical Sciences, Little Rock, AR

Multiple myeloma (MM) is a cancer of the bone marrow characterized by a malignant transformation of plasma cells (PCs). It is currently incurable but patient overall survival has improved dramatically over the past 15 years. Animal models and molecular profiling have both played critical and complementary roles in these advances. An animal model that provides a human-like bone marrow microenvironment is a valuable tool for growing and studying MM cells. The severe combined immune deficient (SCID) mouse model system allows for the growth of primary MM cells in a human-like bone marrow microenvironment. Regarding molecular profiling, recently our program has begun to transition from microarrays to RNA-seq due to its discovery-based nature, base level resolution, and vastly improved dynamic range, which all facilitates potential for biological insights via the identification of new genes, isoforms, gene fusions, etc. In this study we aimed to explore MM PC engraftment phenomena using a SCID mouse model and RNA-seq by comparing “before” and “after” time points. A patient’s bone marrow aspirate derived PCs were evenly divided (i.e., before/baseline, and after animal model engraftment). One half of the cells were then injected into a rabbit bone grafted to a SCID mouse (SCID-rab model) and later harvested (aka “after”). mRNA were separately isolated from both “before” and “after” specimens, two cDNA libraries built, and all experiments were run on an Illumina HiSeq-2000 in an identical manner utilizing 101 bp PE sequencing. The Tuxedo suite was utilized for RNA-seq data analysis and all experiments were processed in an identical manner using a standard pipeline protocol. Results will be reported concerning computational strategies for analyses and visualization, as well as biological insights on genes and isoforms with a particular focus on eight key MM genes, CCND1, CCND3, DKK1, FGFR3, MAF, MAFB, NFKB, and WHSC1.
Chemotherapy-induced alopecia has been well documented as a cause of distress to patients undergoing cancer treatment. The fusion protein of PTH and bacterial collagen binding domain (PTH-CBD) reduced chemotherapy-induced damage of hair follicles in mice and may show promise as a therapy for chemotherapy-induced alopecia (Katikaneni et al. Int J Cancer 2012). Distribution studies of PTH-CBD confirmed uptake of PTH-CBD into the skin at 1 and 12 hr after subcutaneous injection. Two prototypical collagen-binding segments have thus far been used for the applications. Preclinical outcomes differ greatly depending on which collagen binding segment was used. Structural work and cross-linking studies are initiated to elucidate the targeting mechanism of the prototypical segments. To provide structural framework of prototypical collagen binding segments, crystal structures of two CBDs and three polycystic kidney disease-like domains (PKDs) that assist in collagen binding were determined in my lab at high resolution (<2.0 Å). Furthermore, their low-resolution envelopes were determined using small angle X-ray scattering. The crystal structures were built into the envelope to provide their average solution structure and initial insight into how PKD-like domains assist in collagen binding. The results thus far suggest that each prototypical collagen binding segment binds very differently to collagen fibril. A method is also being developed to map the collagen-binding sites on type I collagen fibril, and subsequently, control the application of CBD. Collagen regulates cell functions via receptors on the cell surface and interacts with other matrix proteins. Our current goal is to elucidate the binding sequence on tropocollagen using a site-specific photo-crosslinking strategy combined with mass spectrometry. Putative binding sequences have been identified.

Human Metapneumovirus (hMPV), is a paramyxovirus considered a major respiratory pathogen responsible for up to 15% of low respiratory tract infections hospitalizations in infants and young children. It is also causes bronchiolitis and pneumonia. Currently, there is not vaccine available against hMPV. Knowledge of the critical aspects of the host immune response is crucial to understanding the pathology associated with hMPV infection. We have recently found that hMPV induce type III interferon (IFN). However, the role of this antiviral cytokine in hMPV infection is unknown. In this work, we investigate the production of IFN-lambda in vitro and in vivo using lung epithelial cells and an experimental mouse model of infection. Our data indicate that hMPV induce IFN lambda in epithelial cells in vitro and its production is dependent of viral replication. hMPV is susceptible to the activity of the three isoforms of IFN-lambda. In the mouse model, we observed that hMPV induced IFN-lambda in vivo. Moreover, treatment of mice with IFN-lambda prior hMPV infection resulted in a reduced lung virus titer and a decreased number of inflammatory cells in the lung. Overall, these findings highlight the importance of the interferon responses in hMPV infection and suggest that IFN lambda play a role in the antiviral immune response to paramyxovirus infection.
Control of acute blood-stage Plasmodium chabaudi AS infection is T cell-mediated; however, an antibody-mediated response is necessary to restrict chronic parasitemia to sub-patent levels. High-affinity antibody production takes place in germinal centers (GC), zones of B cell hyperproliferation that form within the follicles of secondary lymphoid organs. Within the GC, CD4+ follicular helper T (TFH) cells promote B cell survival, and facilitate somatic hypermutation and affinity maturation. Expression of the transcriptional repressor Bcl6 and the chemokine receptor CXCR5 are critical for the development of TFH cells. The inducible T cell co-stimulator (ICOS), a member of the CD28 superfamily, has been shown to promote TFH differentiation by inducing Bcl6 and CXCR5 expression. Here we demonstrate that the absence of ICOS did not impair early TFH cell development after infection with P. chabaudi AS, as Icos-/- T cells were capable of expressing Bcl6 and CXCR5. However, by day 11 post-infection, total TFH cell numbers had decreased substantially in Icos-/- mice compared to wild-type mice. Consequently, at day 21 post-infection, total GC B cell numbers were substantially reduced in Icos-/- mice. Treatment of wild-type mice with anti-ICOSL antibody beginning at day 6 post-infection successfully reduced TFH cell and GC B cell numbers by day 21 post-infection, thus recapitulating the phenotype seen in the Icos-/- mice. Additionally, co-transfer of TFH cells derived from day 6 infected wild-type and Icos-/- mice into nude mice indicated that wild-type TFH cells were unable to support expansion and/or long-term maintenance of Icos-/- TFH cells, suggesting a cell-intrinsic role for ICOS in development of a TFH cell response after day 6 of the infection. Collectively, these data suggest that ICOS is not required for early TFH cell induction, but does provide signals necessary for TFH cell proliferation and/or maintenance during resolution of acute P. chabaudi AS infection.

Functional Hierarchy of HSV-1 Membrane Proteins in Corneal Infection and Virus Transmission to Ganglionic Neurons

Ahmad Saied
Graduate Student, Louisiana State University
asaied@lsu.edu

Ahmad Saied, Injoong Kim, Vladimir N. Chouljenko, Ramesh Subramanian, Konstantin G. Kousoulas

HSV-1 viral glycoproteins gK, gM, gE and the membrane protein UL11 are involved in virus assembly, egress and virus spread. To determine the relative importance of each of these proteins in infection of ganglionic neurons following infection of mouse corneas, we constructed and tested in a mouse model system recombinant viruses lacking expression of each protein. The gK-null virus produced the smallest viral plaques on Vero cells followed by the UL11-null, gE-null, and gM-null viruses. The ability of each virus to replicate in mouse corneas, produce ocular disease, and infect trigeminal ganglia was tested via infecting mouse eyes after corneal scarification. Mice infected with the wild-type virus exhibited mild blepharocconjunctivitis and ocular discharge at 7 days post infection. In contrast, mice infected with the recombinant viruses did not show significant ocular changes. The wild-type virus produced the highest titers of viral shedding from infected corneas followed by the gM-null, gE-null, UL11-null, and gK-null viruses. High numbers of viral DNA genomes were detected in 100% of the trigeminal ganglia collected from mice infected with the wild-type virus. In contrast, low-to-moderate numbers of viral genomes were detected in the trigeminal ganglia of mice infected with the gE-null and gM-null viruses, while no viral genomes were detected in the trigeminal ganglia of gK-null infected mice. Interestingly, 60% of mice infected with the UL11-virus contained moderate numbers of viral genomes in their ganglia. Collectively, these results show that gK plays the most important role in corneal and ganglionic infection in the mouse model followed by gM, gE and UL11 in a descending order of importance relative to wild-type virus infection.
Vaccination with the HSV-1 Attenuated Virus VC2 Protects Mice against Lethal Challenge with Virulent HSV-1 and HSV-2 strains

Brent Stanfield  
Graduate Student, Louisiana State University  
brentstanfield@gmail.com

Brent Stanfield, Vladimir N. Chouljenko, Jason D. Walker, Jacquie Stahl, Ahmad Saied, Anu Charles, Konstantin G. Kousoulas

Herpes Simplex Virus type 1 (HSV-1) and type-2 (HSV-2) establish life-long infections and cause significant orofacial and genital infections in humans. HSV-1 is the leading cause of infectious blindness in the western world. Currently, there are no available vaccines to protect against herpes simplex infections. Our working hypothesis is that HSV-1 mutant viruses that lack functional glycoprotein K (gK) can be used for vaccine purposes, based on our published work that gK is an important determinant in neuronal infection and establishment of latency in ganglionic neurons in mice. Recently, we showed that a single intramuscular immunization with an HSV-1(F) mutant virus lacking expression of the viral glycoprotein K (gK) conferred significant protection against either virulent HSV-1(McKrae) or HSV-2(G) intravaginal challenge in mice. Specifically, 90% of the mice were protected against HSV-1(McKrae) challenge, while 70% of the mice were protected against HSV-2(G) challenge. We sought to improve on these vaccine results by engineering a virus that replicated efficiently in cell culture, while unable to efficiently infect neurons. Thus, we constructed the recombinant virus VC2 that contains specific mutations in gK and the membrane protein UL20. The VC2 virus replicates efficiently in cell culture, unlike the gK-null virus. Intramuscular injection of mice with 107 VC2 plaque forming units did not cause any significant clinical symptoms in mice. A single intramuscular immunization with the VC2 virus protected 100% of mice against lethal intravaginal challenge with either HSV-1(McKrae) or HSV-2(G) viruses. The VC2 vaccine produced high HSV-1 specific antibody titers and HSV-1/HSV-2 cross-reactive cell mediated immune responses. These results suggest that the VC2 virus is safe and efficacious vaccine in mice. The VC2 virus can be effectively utilized as a vaccine vector for the production of vaccines against other viral and bacterial pathogens.

Defining a New Operon, msa, and its Role in Biofilm Development and Virulence

Gyan S. Sahukhal  
Graduate Student, University of Southern Mississippi  
gyan.sahukhal@eagles.usm.edu

Gyan S. Sahukhal, Mohamed O. Elasri, University of Southern Mississippi

Emergence of community-acquired methicillin resistant Staphylococcus aureus (CA-MRSA) strains is causing severe infections among healthy individuals without predisposing risk factors outside the hospital setting with different clinical syndrome and with different antimicrobial susceptibility is alarming. The fundamental key behind the success of these strains is their ability to quickly respond to environmental conditions by differentially regulating genes. Previously we identified the msa gene as a global regulator in S. aureus. In this study we define a new operon that contains the msa gene in CA-MRSA clinical strain USA300 LAC. We used several techniques to define the msa operon. Transcript analysis by SMARTerTM RACE cDNA amplification assay to find the transcription start and end shows that msa gene is part of a three-gene operon. RT-qPCR analysis of the expression of the three open reading frames and their intergenic regions also confirmed the structure of the msa operon. We used allelic replacement method to delete the putative msa operon and studied different phenotypes of the mutant. We studied biofilm formation under static and flow conditions and examined the structure and composition of biofilm using confocal microscopy. Deletion of msa operon down-regulates the expression of global regulators including sarA, and agrA by 7.72 and 16.56 fold respectively. Deletion of the msa operon resulted in a significant increase in Triton-X 100-induced autolysis and a significant reduction in biofilm formation. The mutant also showed 4.5 fold decreased pigmentation and 5.35 fold increased extracellular protease activity. These results show that msa operon plays a key role in autolysis, biofilm development and regulation of virulence genes. The identification of this operon and expression of the three open reading frames will allow us to define the mechanism of action of this locus. This will augment our understanding of the regulatory network in S. aureus.
Poster Session Abstracts
Investigation of the Mechanism of Apparent HPLC Solvent Interference with an Avidin-Binding Assay

Katelyn Robillard
Undergraduate Student, Southeastern Louisiana University
katelyn.robillard@selu.edu

Katelyn Robillard, Anna Bogusiewicz, Nell Matthews, and Donald Mock; Department of Biochemistry and Molecular Biology, University of Arkansas for Medical Sciences

Biotin, also known as vitamin B7, is an essential coenzyme involved in human metabolic reactions. In studying vitamin deficiencies in newborns, pregnant women, and other adults, a variety of techniques are employed to quantitate biotin and biotin metabolites in biological samples. One of these techniques involves HPLC separation of the metabolites followed by an avidin-binding assay. In recent months, we have observed apparent contamination in the baseline HPLC fractions; these contaminants interfere with quantitation of biotin and biotin metabolites. Both mobile phases of the HPLC gradient exhibit the interference, and both use trifluoroacetic acid (TFA) as the buffer. We hypothesized that the contamination arises from a degradation product of TFA that has avidin-binding characteristics and could be removed by avidin dialysis. Avidin is a tetrameric protein found in the white of chicken eggs. Each avidin molecule forms tight, non-covalent bonds with four molecules of biotin. Our initial study compared the amount of TFA contamination before and after avidin dialysis. Contamination increased after treatment, which is inconsistent with our hypothesis that the contamination should be removed by avidin. Next, we assessed the biotin-binding capacity of avidin in TFA solution (pH 2.2) and compared that to biotin-binding capacity of avidin in water (pH 7.0). Based on assessing the binding of [3H]biotin by dialysis, avidin bound biotin less effectively in TFA than water. Interpretation: The low pH environment of TFA caused denaturation of avidin (unfolding of quaternary and tertiary structures). Conclusion: Avidin is unsuitable for removing the contamination in TFA. In the future, we plan to design a method for removing this contaminant, to define the timing needed for removal, and to investigate conditions that minimize the contamination (e.g., reduce the concentration of TFA).

G4 quadruplexes in mitochondrial DNA: a bioinformatics study of their origin, function, and evolution

Boris L Zybailov, Ph.D.
Instructor, University of Arkansas for Medical Sciences
BLZybailov@UAMS.edu

Boris L Zybailov, 1Department of Biochemistry and Molecular Biology, University of Arkansas for Medical Sciences, Little Rock, AR

G4 quadruplex consists of stacked guanine tetrads held together by Hoogsteen-bonding. Recent evidence suggests G4 involvement in genome maintenance and repair. Quadruplex-forming potential of a given sequence depends on the number of stacked G-tetrads, length and flexibility of the loops, as well as presence of monovalent cations; and can be assessed computationally. G4 quadruplexes in nuclear genome has been well-studied by both computational and experimental methods. G4 has been shown to be overrepresented in telomeres and hot-spots of double-stranded DNA breaks. The idea of G4 function being related to DNA damage-processing has been reinforced even further by analysis of G4-forming sequences in radiation-resistant bacteria Deinococcus radiodurans. Supposedly, mitochondrial DNA (mtDNA) is subject to more genotoxic stress compared to the nuclear DNA, both because of the increased concentration of reactive oxygen species, and absence of protective histones. Interestingly, concentration of G4-forming sequences is higher in mitochondria (several fold compared to nuclear DNA). In the current study we explore the following questions: i) How G4s are distributed in mtDNAs amongst different eukaryotic species? ii) Are there any conserved G4-sequences; and are there any conserved G4 positions within mtDNA?; iii) Are there any G4-sequences also occur in nuclear genomes? In this work we employed publically available software and various online tools such as Mitozoa, QGRS-mapper, and BLAT (Blast-like alignment tool). Our results indicate higher densities of quadruplexes in heavy strand of Mt-DNA in comparison to the light strand. Among the coding genes, most of the quadruplexes are present in protein coding genes rather than in tRNAs and rRNAs. We also uncovered several instances where mtDNA quadruplex was also present in nuclear genome of the same species. Genomic context of these sequences was also investigated using analysis of NUMT tracks with UCSC genome browser.
Identification of novel sarco/endoplasmic reticulum calcium ATPase (SERCA) inhibitors utilizing QSAR modeling

Emily Hofmann
Undergraduate Student, Northern Kentucky University
hofmanne1@nku.edu

Emily Hofmann, Stefan Paula, Department of Chemistry, Northern Kentucky University; John Burden, Procter & Gamble Company; David Stanton, School of Natural Sciences, Spalding University

Selective inhibition of the sarco/endoplasmic reticulum calcium ATPase disrupts the enzyme's ability to transport ions across the reticular membrane thus upsetting calcium homeostasis within the cell. Agents capable of inhibiting SERCA at low micromolar concentrations may have potential as prodrugs targeting prostate cancer. Using data from previous studies of SERCA inhibitors, three quantitative structure-activity relationship (QSAR) models were independently developed using different methodologies. Several commercial databases were then virtually screened for novel inhibitors using the newly developed QSAR models. Sixteen compounds were selected and tested in the laboratory with an inhibition activity assay and cell based fluorescence bioassays. Six of these compounds demonstrated excellent potencies in the low micromolar range and five more showed inhibition at millimolar concentrations. The experimental results were then incorporated into a comprehensive master QSAR model, whose physical interpretation by partial least squares analysis revealed that properly positioned substituents at the central phenyl ring capable of forming hydrogen bonds and of undergoing hydrophobic interactions were prerequisites for effective SERCA inhibition.

Gene Set Net Correlations Analysis (GSNCA): A multivariate differential coexpression test for gene sets

Galina Glazko
Assistant Professor, University of Arkansas for Medical Sciences
gvglazko@uams.edu

Galina Glazko, Rahmatallah Y.1, Emmert-Streib F.2 1 Division of Biomedical Informatics, University of Arkansas for Medical Sciences, Little Rock, AR 72205. 2Computational Biology and Machine Learning Laboratory, Center for Cancer Research and Cell Biology, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, 97 Lisburn Road, Belfast, BT9 7BL, UK.

Motivation: To date, Gene Set Analysis (GSA) approaches primarily focus on identifying differentially expressed gene sets (pathways). Methods for identifying differentially coexpressed pathways also exist but are mostly based on aggregated pairwise correlations, or other pairwise measures of coexpression. Instead, we propose Gene Set Net Correlations Analysis (GSNCA), a multivariate differential coexpression test that accounts for the complete correlation structure between genes. Results: In GSNCA weight factors are assigned to genes in proportion to the genes' cross-correlations. The problem of finding the weight vectors is formulated as an eigenvector problem with a unique solution. GSNCA tests the null hypothesis that for a gene set there is no difference in the weight vectors of the genes between two conditions. In simulation studies and the analyses of experimental data we demonstrate that GSNCA, indeed, captures changes in cross-correlations rather than differences in the average coexpressions/correlations of the genes. Thus, GSNCA infers differences in coexpression networks, however, bypassing computer-intensive and method-dependent steps of network inference. As an additional result from GSNCA, we define hub genes as genes with the largest weights and show that they correspond frequently to major and specific pathways regulators, as well as to genes that are most affected by the biological difference between two conditions. In summary, GSNCA is a new approach for the analysis of differentially coexpressed pathways that also evaluates the importance of genes in pathways thus providing unique information that may result in new biological hypotheses.
Discovery and Bioinformatic Analysis of Mycobacteriophages Achebe, MooMoo, Simpliphy and Updawg

Gretchen A. Walch
Undergraduate Student, Western Kentucky University
gretchen.walch015@topper.wku.edu

Mycobacteriophages Achebe, MooMoo, Simpliphy and Updawg were isolated and characterized by students in the Genome Discovery and Exploration course at Western Kentucky University. Achebe is a member of the A4 subcluster of mycobacteriophages and exhibits small clear plaques. Achebe particles have hexagonal capsids that are approximately 62 nm in diameter and tails that are approximately 146 nm long. The genome is 51,433 bp and includes a 10 bp 3’ overhang (CGGCCGGTTA). It has 84 predicted genes and is most similar to bacteriophages Backyardigan and Wile. MooMoo was isolated from a water sample taken from a creek of clear running water along with some sediment from the creek bed. It produces plaques with bullseye morphology. It has an unusual elongated capsid that is 25 nm in diameter and 129 nm in length. Its tail is 234 nm long and its genome is 55,178 bp and includes a 9 bp 3’ overhang (CCCGCCTGA). It has 99 predicted genes, three of which have very dissimilar or no BLAST matches. Although MooMoo is genetically most similar to the F2 subcluster of mycobacteriophages, its morphology is most similar to the cluster O mycobacteriophages. Bacteriophage Simpliphy is a member of the E cluster of mycobacteriophages and produces plaques with clear centers and turbid margins. Simpliphy’s genome is 75,363 bp without a 3’ overhang. It has 140 predicted genes and 2 tRNAs. The phage particles have hexagonal capsids that are 54 nm in diameter and tails that are 203 nm in length. Bacteriophage Updawg is a member of the A2 subcluster of mycobacteriophages and exhibits extremely turbid plaques. Its genome is 53,025 bp without a 3’ overhang. The phage particles have hexagonal capsids that are 50 nm in diameter and tails that are 110 nm in length. Its genome has 96 predicted genes and 1 tRNA. Our results support the idea that bacteriophage populations are diverse.

Assessing associations between idiosyncratic reactions-causing drugs and HLAs via computational approaches

Heng Luo
Graduate Student, University of Arkansas at Little Rock
hxluo@ualr.edu

Idiosyncratic drug reactions (IDRs) are known as Type B adverse drug reactions (ADRs) which are hard to predict and caused a significant number of deaths in US hospitalized patients, as well as withdrawals and terminations of on-market drugs. Many IDRs are so rare in the vast population that they are not detectable during the clinic trials; however, they may lead to fatal results once occurred. Containing a variety of alleles and mutations, human leukocyte antigen (HLA) is one of the important genetic factors to cause drug-induced adverse reactions. In order to understand the associations between HLAs and IDRs, we first collected the literatures about HLA-related IDR reports to build an in-house database, and then we implemented modeling and docking approaches to assess the interactions and associations between HLAs and drugs. With the help of Chemical-Protein Interactome (CPI), we analyzed the characteristics of the IDR-causing drugs and HLAs via their docking profiles, and explored the possibilities to predict their interactions based on the in silico approaches. By the combination of both the literatures and computer-simulated data, we hope to understand the insights of HLA-related IDRs better and finally predict the potential IDR risks for patients given specific HLA alleles.
Pharmaceutical drugs are activated through a process called xenobiotic metabolism. Out of the drugs on the market, 50% are chiral, having two enantiomers. When this drug is metabolized, one of the enantiomers is typically preferred over the other. This unique specificity is thought to be a result of the structure of the protein. Interactions between different residues and the drug being metabolized could affect the movement and orientation of the drug as it moves down the channel of the protein to be oxidized. Further understanding of the metabolism of chiral drugs could be used to predict how new drugs would react within a protein. The results were determined using computational methods. Molecular dynamics in Sybyl-X 1.3 were used to create a simulation of the first step in an oxidation reaction between a drug and a protein. The final product was analyzed to determine the interactions of close residues and calculate their stabilizing energy. The residues with the largest difference in energy between enantiomers were determined for each of the four chosen chiral drugs. This data was compiled with previous research to pinpoint residues possibly responsible for enantiospecificity in CYP2C9.

BI18 Observation of Enantiospecificity in CYP2C9 Using Computational Methods

Mallory Burroughs
Undergraduate Student, Ouachita Baptist University, Arkansas
bur51519@obu.edu

Mallory Burroughs, Grover P. Miller, University of Arkansas for Medical Sciences Martin D. Perry, Jr., Ouachita Baptist University

About half of the drugs on the market today express chirality, possessing two enantiomers. Often, one enantiomer of a drug metabolizes better than the other. CYP2C9, a sub-family of the super-family of proteins Cytochrome 450, demonstrates strong enantiospecificity. Using Tripos Sybyl-X software, observations of these drugs interactions with residues within the enzyme CYP2C9 during metabolism could support hypotheses that certain residues play a large role in CYP2C9’s selectiveness. Computational docking methods, including molecular dynamics, aid in the examination of drug metabolism. Molecular dynamics simulates the docking of each drug and initial steps of an oxidation reaction. After interactions are identified, calculations of residue energy for each reaction are calculated. These properties and calculations are compiled with past research data to find which residues are contributing to the enantiospecificity. With further understanding of CYP2C9’s structure, additional research can be done to advance the process of releasing drugs onto the market. This study assesses four drugs: Lansoprazole (proton pump inhibitor), Ketoprofen (anti-inflammatory), Acenocoumarol (anti-coagulant), and Citalopram (anti-depressant).

BI19 Computational docking and analysis of pyrazole derivatives in CYP2E1

Martin D. Perry, Jr., Ph.D.
Professor, Ouachita Baptist University, Arkansas
perrym@obu.edu

Martin D. Perry, Jr., Joseph W. Levy, Ouachita Baptist University Grover P. Miller, University of Arkansas for Medical Sciences

CYP2E1, a member of the cytochrome P450 super family of monooxidases, has been shown to metabolize a variety of small, nonpolar, cyclical compounds. The drug design and administration community are particularly interested in CYP2E1 for its ability to metabolize drugs into inactive or carcinogenic forms. CYP2E1 is of special interest for its novel substrate inhibition kinetics with unknown physiological implications. To investigate both CYP2E1’s substrate inhibition and metabolic mechanism, a series of computational tests involving a combination of Surflex-Dock and molecular dynamics on a Sybyl-X 1.3 Mac platform were conducted. Docking was simulated with eight pyrazole inhibitors. Channel fluctuation and energy measurements suggested the existence of two choke points within the channel: at the opening and near the ligand-binding domain. The results also indicated that several residues assisted the docking and orientation of the incoming ligand by the formation of stabilizing hydrogen bonds, including: Phe207, Ser209, Leu210, Trp214, Thr303, Phe298, Phe298, and Phe478. The study also illuminated the nuances in the functional role of Thr303 in the docking of ligands with a polarized group that both aided and inhibited ligand docking. All of the above results indicated that CYP2E1 has many mechanisms by which it exhibits selectivity and specificity for its substrates.
BI20  Extending an ontology for biobank administration to cover data related to studies, study participants and specimens

Mathias Brochhausen, Ph.D.
Assistant Professor, University of Arkansas for Medical Sciences
mbrochhausen@uams.edu

Mathias Brochhausen, Alice Nzinga (First author), UALR Kashif Mehdi (Second author), UALR, Umit Topaloglu (Third author), Division of Biomedical Informatics, University of Arkansas for Medical Sciences

A Bio-repository consists of biological specimens and associated information for the purpose of future use in research. Bio-repositories exist in many different countries, are run by many different institutions and store specimens and specimen data for a multitude of different usages. Due to this, numerous data schemas and terminologies are used to annotate and structure the data. This results in a lack of semantic interoperability and usability of bio-specimen data. The EU-funded Bio-bank and Bio-Medical Research Infrastructure (BBMRI) aimed to alleviate these problems by providing a common data schema, the Minimum Information About Biobank data Sharing (MIABIS). In a previous effort MIABIS was transformed into an ontology of biobank administration (OMIABIS). The primary goal of our research is to extend OMIABIS to cover data about studies, data about study participants and data about specimens. The extension follows the methodology outlined by OMIABIS: It is coded in web ontology language (OWL) and is consistent with the Open Biological and Biomedical Ontologies Foundry’s principles. We use the Protégé Ontology Editor to extend OMIABIS. The result of the research is a new version of OMIABIS, which contains classes representing entities related to studies, study participants and specimens. In addition, we ensure that the coverage includes entities from tissue procurement forms used at our institution. This ontology improves the usability of the data by allowing logic-based reasoning in complex data queries. It provides a formal, semantic representation of the domain, fostering data integration across different bio-repositories. In future work we will annotate data captured through tissue procurement forms with unique resource identifiers (URIs) from OMIABIS. Thus, the data collected gets linked to the ontology and can be 1) automatically reasoned with and 2) compared and integrated with data from other sources annotated with the same ontology.

BI21  3D Structure Model of the Chloroplast Signal Recognition Particle

Mercede Furr
Graduate Student, University of Arkansas
mfurr@email.uark.edu, sjayanth@uark.edu

Mercede Furr, R. Henderson1, M. Furr1, S. Jayanth1, A. Kight2, A. Cox2, F. Gao1 (Please check name), C. Heyes1, R. Goforth2, R. Henry2, and T. K. S. Kumar1 1. Department of Chemistry. 2. Department of Biological Sciences University of Arkansas, Fayetteville, AR 72701

The chloroplast signal recognition particle (cpSRP) is a heterodimer consisting of 54 kDa and 43kDa. subunits. cpSRP mediates the post-translational targeting of the Light Harvesting Chlorophyll Binding Protein (LHCP) to the thylakoid membrane. In this study, we report the successful in silico modeling of the three-dimensional structure of cpSRP using sophisticated molecular modeling techniques. The 3D structure model of cpSRP exhibits a low and favorable Lennard-Jones energy. PROCHECK validation produced excellent Ramachandran statistics suggesting that the 3D structure of cpSRP is of high quality. Results of FRET experiments are in good agreement with the structural features deduced from the 3D structure model of cpSRP. The structure of cpSRP reveals that cpSRP43 subunit is L-shaped and has direct structural contacts with the M-domain of the cpSRP54 subunit. Interestingly, the M-domain contains a prominent hydrophobic pocket which potentially can serve as a binding interface for the non-polar signal peptides as well as for the transmembrane helices of LHCP. The predicted role of the hydrophobic pocket was tested by introducing mutations in the M-domain of full-length cpSRP54. In support of the model, these mutations eliminated the ability of cpSRP54 to support formation of a cpSRP-LHC targeting complex, but had no influence on cpSRP assembly as judged by the ability of each cpSRP54 mutant to bind cpSRP43 with the same efficiency as wild type cpSRP54. The 3D structure model of cpSRP is not only consistent with the available information on the structural and functional properties of cpSRP but it also provides novel insights on the molecular mechanism underlying the post-translational targeting of LHCP.
BI22  Genomic code for Nucleosome positioning is evolutionarily conserved from archaea through man

Narismha Nalabuthula, Ph.D.
Post Doctoral Fellow, University of Kentucky
y.fondufe-mittendorf@yahoo.com

Narismha Nalabuthula, Yvonne Fondufe-Mittendorf

Packaging of DNA into nucleosomes almost certainly evolved in the Archaea, and predates Eukaryotes. We showed earlier that eukaryotic genomes encode an additional layer of genetic information that controls the positioning of nucleosomes, directed by primary sequence motifs that together form a nucleosome positioning code. We tested if this information evolutionarily conserved. We undertook experiments to determine if archaeal histone assembly conforms to the nucleosome positioning code. Deep sequencing of genomic DNA protected from micrococcal nuclease digestion by assembly into archaeal nucleosomes established that archaeal nucleosome assembly is also directed and positioned by similar DNA sequence motifs, both in vivo in Methanothermobacter thermautotrophicus and Thermococcus kodakarenis and in vitro in reaction mixtures containing only one purified archaeal histone and genomic DNA. Archaeal nucleosomes assembled at the same locations in vivo and in vitro, with much reduced assembly immediately upstream of open reading frames and throughout the ribosomal rDNA operons. We provide further support for a common positioning code, showing that archaeal histones assembled into nucleosomes on eukaryotic DNA and eukaryotic histones assembled into nucleosomes on archaeal DNA at the same locations. The results obtained establish that an archaeal histone and a genome sequence together are sufficient to determine where archaeal nucleosomes preferentially assemble and where they avoid assembly. We confirm that the same nucleosome positioning code operates in Archaea as in Eukaryotes and presumably therefore evolved with the histone-fold mechanism of DNA binding and compaction early in the archaeal lineage, before the divergence of Eukaryotes. We are currently studying whether archaea just like eukaryotes, utilize this code to facilitate specific facilitate specific chromosome functions.

BI23  MotifBrowser: Robust High-Throughput Genome-Wide Mining and Exploration of Motifs

Phillip C. S. R. Kilgore, Ph.D.
Post Doctoral Fellow, Louisiana State University Shreveport
pkilgore@lsus.edu

Phillip C. S. R. Kilgore, Urska Cvek (LSU Shreveport), Phoebe A. Rollyson (LSU Health Shreveport), Rona S. Scott (LSU Health Shreveport), Marjan Trutschl (LSU Shreveport)

Modern sequencing technology has permitted the collection of extensive sequence data. Complete genomes for over 2700 species exist right now, and will grow through initiatives such as the 10K Genome Project. This is a boon for life scientists who are interested in motif extraction to identify novel phylogenetic relationships, to locate regulatory elements that facilitate transcription factor binding, or to predict secondary structure. However, it also presents computational and processing challenges. We present a method of genome-wide mining of sequence motifs. Our pipeline begins by extracting sequences in the [-1000, 4000] interval of each gene’s sequence, ensuring that potential promoter regions are captured. We then supply these data to Dispom, a tool for the de-novo discovery of differentially abundant transcription factor sites, to construct a database of candidate motifs. We partition the genome into randomly-assigned bins to serve as input for independent Dispom processes executed on a 312-core computational cluster, and then use a high-pass frequency filter to remove outliers. We then construct a greedy prefix tree from the motif database in order to find the exact location (hit) of each motif within the sequence. We also introduce the concept of an “implied hit” to allow for the possibility that some motifs may be super-sequences of simpler, known motifs. We provide a database-driven interface to allow for multiple views of the data. Users may supply a list of various identifiers in order to obtain a report restricted to the genes of interest, may browse a motif for genes associated with it, or may obtain all of the motifs for a single gene. Initially, we used the GRC37h reference assembly and identified several candidate motifs of high variation, length, and frequency. In the future, we will expand this project with data from other species to allow for phylogenetic inferences.
Obesity is an ever growing health problem in many regions of the world. Cytosolic malic enzyme (ME1) plays an important role in insulin induced lipogenesis as it has been observed to be one of the major sources of NADPH for de novo fatty acid synthesis. Malate, an important Krebs cycle intermediate is exported from the mitochondria to the cytosol, where malic enzyme regenerates pyruvate from malate which is again cycled back to the mitochondria. It is evident from previous research that high activity cytosolic malic enzyme is responsible for a large part of pyruvate cycling. This cycle has been hypothesized of being a necessary component of glucose-stimulated insulin secretion. Also, increased insulin signaling in liver and adipose tissues leads to higher accumulation of fat mass and higher risk for obesity, effects also mediated by ME1. Thus ME1 may be a good drug target to combat obesity. The protein–ligand docking process involves computationally predicting the likelihood of small drug like molecules binding into the active site of the enzyme. Computer-aided drug design techniques were used to identify ME1 inhibitors with therapeutic value. For the current work, the human ME1 3-dimensional model was obtained from the Swiss-Model repository. As the model lacked co-factor NADP, it was added to the structure using the available pigeon ME1 crystal structure. Software package SYBYL was used for identification of the active site surface and probable amino acids on the active site that would interact with the inhibitors. Virtual screening techniques were used to mine through large databases (ZINC-UCSF) containing drug-like molecules to identify lead molecules that fit into the active site. The molecules obtained were used for docking using software packages SURFLEDDOCK (SYBYL) and AutoDock Vina (Scripps Research Institute) were used for this purpose. The molecules having low binding energy score were identified and these will be further analyzed using in vitro assays.
**BI26**  
An alternative method for analyzing NanoString data

Shu Shen  
Graduate Student, University of Kentucky  
shu.shen@uky.edu

Shu Shen, Stromberg, Arnold

NanoString provides a new method to measure gene expression in RNA samples. It's more sensitive than microarrays and able to do more gene measurements than RT-PCR with similar sensitivity. This system produces counts for each target gene and tabulates them. Counts in those tables can be normalized before analysis. NanoString suggests normalization be performed in three steps: positive control normalization, reference gene normalization and background correction. NanoString provided an Excel macro to perform these normalizations. Recently, NanoString has introduced nSolver as a replacement for the Excel macro. NanoString relies on data normalization prior to statistical analysis to identify differentially expressed genes. Alternatively, we propose to model gene expression as a function of positive control, negative control and reference gene measurements. Simulations and examples compare our method with Nanostring methods for identifying differentially expressed genes. In some cases, our method provides far more reasonable gene lists.

---

**BI27**  
Influence of pH and Side Chain Glutamic Acid on the Behavior of Designed Transmembrane Peptides in Lipid Bilayers

Venkatesan Rajagopalan  
Graduate Student, University of Arkansas  
vxr004@uark.edu

Venkatesan Rajagopalan, Denise V. Greathouse and Roger E. Koeppe II  
Department of Chemistry and Biochemistry, University of Arkansas, Fayetteville, AR 72701

GWALP23 (acetyl-GGALW5LALALALALALALW19LAGA-amide) is an advantageous model peptide for investigations of single-residue effects on protein-lipid interactions and the properties of membrane-spanning helices (J. Biol. Chem. 285, 31723). GWALP23 has favorable properties in bilayer membranes because the peptide exhibits only limited dynamic averaging of NMR observables such as the 2H quadrupolar splitting or the 15N-1H dipolar coupling (Biophys. J. 101, 2939). To investigate the potential influence of negatively charged glutamic acid side chains upon system properties, we have substituted a single Leu residue with Glu at different positions and incorporated specific 2H-Ala labels in the core transmembrane sequence. For fluorescence experiments, we employ a single Trp reporter (W19) in the peptide Y5GWALP23 (see Biochemistry 51, 2044). Solid state 2H NMR experiments were used to examine the peptide orientation and dynamics as functions of the lipid bilayer thickness and pH in hydrated lipid bilayer membranes. We observe well defined 2H quadrupolar splittings for Y5GWALP23-E16 in the pH range from 4.0 to 8.2, suggesting that the peptide helix is well oriented in DOPC lipid bilayers, probably with the E16 side chain protonated (neutral). At pH 2.5, we observe multi-state behavior, perhaps due to degradation when the bilayers are composed of ester lipids. Above pH 8.2, the deprotonation of E16 seems to have little if any effect on the peptide orientation, perhaps suggesting that the close proximity of E16 to W19 (on the next helical turn) could provide stability to the peptide helix and influence global properties. We are also studying the peptide-lipid behavior when Glu is substituted in position 12 and/or 14, individually or together.
What is information: A representational view and its implications

William R. Hogan, M.D., M.S.
Professor, University of Arkansas for Medical Sciences
wrhogan@uams.edu

We hold that information at its core essence is a type of representational artifact, which represents some part of reality (usually other than itself) at a particular time point or interval. This definition states necessary but not sufficient criteria, because representational artifacts that are not information also satisfy the definition. For example, photographs, paintings, drawings, plays, etc. also represent some part of reality at a point or interval in time, but are not information per se. Images and videos such as X-rays and fetal ultrasounds are perhaps borderline cases: many clinicians would say at minimum that they contain information about a patient. Nevertheless, we restrict our treatise here to representational artifacts that are symbolic. By symbolic, we mean that the artifact is codified in graphical symbols such as numerals, letters, other characters, etc. that can be written down, drawn on a computer screen, etc. Thus, this abstract is information. Note that fiction is excluded from our definition because it is not representational: it does not represent the state of the world at a time. This definition of information—which if it is not novel then it is at least not widely used or recognized—has several implications for the theory and practice of informatics. In particular there are implications for information creation, interpretation, and encoding as well as information quality that I will discuss.

Database of Uca minax transcriptome

Casey Cole
Undergraduate Student, University of South Carolina
homayoun@cec.sc.edu

Casey Cole, University of South Carolina, Arjang Fahim, University of South Carolina, Hanin Omar, University of South Carolina, Giuliana Gusmaroli, University of South Carolina Beaufort, Homayoun Valafar, University of South Carolina

Advances in next-generation sequencing have significantly improved the cost and time requirement of DNA/RNA sequencing. The improvements that are afforded by advances in sequencing techniques present new challenges in assembly of the short sequences (around 100bp), which impede the unleashing of their full potential. Therefore, evaluation and development of new analysis techniques continues to be an international area of investigation. In this report we present evaluation and analysis of one next-generation sequencing data using the widely known program Trinity; an open source, De novo, transcriptome sequencing tool. More specifically we provide a comparison of analysis results based on relational-database queries, blast search mechanism, and Trinity. We apply our analysis to a unique set of transcriptome data obtained from Uca minax, commonly known as the red-jointed fiddler crab.

Study of Uca minax provides a unique opportunity in extending our knowledge of genetic information since the crustacean family is among the groups of organisms sparsely represented in current genomic databases. In the case of Uca minax, next-generation sequencing was conducted on six different tissue samples at the Genomic Lab of the David H. Murdock Research Institute(http://dhmri.org/). A 100 Bp paired end read sequencing run was conducted twice on each individual tissue using the Illumina HiSeq2000 instrument. This yielded 12 files each containing 7360115 sequences in fastq format, each occupying around 1.8G of storage. These files were then parsed using a Perl script and stored in a MySQL database. The use of a relational database considerably improves the efficiency in processing and management of large data sets. In this framework simple database queries can be issued to rapidly reconstruct a portion of the transcriptome.

The data we’ve collected signifies one of the first existing sequences for crustaceans and will serve to sample the gaps in existing genomic data. All processing, analysis and raw data will be made available through our website ifestos.cse.sc.edu.
**CN11** Immuno-virotherapy using myxoma virus to treat ovarian cancer

Jia Liu, Ph.D.
Assistant Professor, Department of Microbiology and Immunology, University of Arkansas for Medical Sciences
jliu4@uams.edu

Jia Liu, Ph.D., Tresor Mukiza, Martin Cannon
Department of Microbiology and Immunology, University of Arkansas for Medical Sciences, Little Rock, AR 72205

Myxoma virus (MYXV) is a rabbit-specific poxvirus. It is an excellent oncolytic virus that can specifically target and kill cancer cells. This has been shown in in vitro and in vivo models such as melanoma, pancreatic, and brain cancer. In addition, MYXV treatment in a murine syngeneic tumor model of pancreatic cancer caused the immune clearance of peritoneal metastases leading to resistance of challenge using the same tumor cells. MYXV can also specifically eliminate cancer cells (e.g., myeloma cells) within the autologous grafts, while not affecting normal hematopoietic stem or progenitor cells, to inhibit tumor engraftments. Finally, MYXV can infect colon cancer stem cells to prevent tumorigenesis. Ovarian cancer (OC) is the gynecologic malignancy with the highest case-to-fatality rate: 69% of patients succumbed to the disease with less than 30% surviving 5 years after diagnosis. In the case of epithelial ovarian cancer (OC), more than 75% of the patients have peritoneally disseminated tumors at the time of diagnosis. Although most patients respond well to the initial chemotherapy treatment, it is the recurrence of chemo-resistant cancer that causes the high fatality rate of this cancer. It is now recognized that the existence of OC stem cells is responsible for the resistance to chemotherapy. This leaves OC patients with few treatment options. In addition, OC tumor cells can also establish an immunosuppressive microenvironment to escape the host immune surveillance, which is associated with the poor prognosis of OC. New therapeutic regimes are urgently needed to treat OC. We proposed a novel approach of immunotherapy using MYXV to specifically tackle this difficult cancer. We mechanistically examine the ability of MYXV to infect and kill primary human OC cells with and without stem cell characterizations. Meanwhile, we will develop and test the oncolytic and immunotherapeutic potential of MYXV in a murine syngeneic OC model with peritoneal dissemination.

**CN12** Quercetin Decreases Tumorigenesis in a Mouse Model of Breast Cancer

E. Angela Murphy, Ph.D.
Assistant Professor, University of South Carolina
angela.murphy@uscmed.sc.edu

E. Angela Murphy, Ph.D., Jennifer L. Steiner, Department of Exercise Science, University of South Carolina, Jamie L. McClellan, Department of Pathology, Microbiology & Immunology, School of Medicine, University of South Carolina
J. Mark Davis, Department of Exercise Science, University of South Carolina, Mitzi Nagarkatti, Department of Pathology, Microbiology & Immunology, School of Medicine, University of South Carolina
Prakash S. Nagarkatti, Department of Pathology, Microbiology & Immunology, School of Medicine, University of South Carolina

Inflammation can contribute to breast cancer (BrCa) initiation, progression and worsened prognosis. Quercetin (Quer) is a flavonol with anti-inflammatory actions that may have important chemopreventive potential. We used a well-characterized mouse model of BrCa to examine the benefits of Quer on tumorigenesis, and further, sought to determine whether Quer exhibited anti-inflammatory actions in this model. Female C3(1)/SV40Tag mice were assigned to a Quer (0.2%) or control (AIN-76A) diet (n=14-15) at 4wks of age and tumor number and volume were recorded bi-weekly. Plasma MCP-1 and expression of macrophage markers and inflammatory mediators were measured in the mammary gland and tumors. We also performed a micro array analysis of mRNA to begin to determine molecular changes following Quer treatment. Quer decreased tumor number (20wks) and volume (18.5-20wks); at sacrifice (20wks) average tumor volume was 2061.8 ± 977.0 mm3 in control mice and only 462.9 ± 75.9 mm3 with Quer treatment. This was consistent with a reduction in invasiveness and numbers of ductal lesions in the mammary gland. Plasma MCP-1 and tumor MCP-1 protein was decreased with Quer (P<0.05). Similarly, markers of pro-tumor macrophages (CD206 and IL-10) were reduced in the mammary gland of Quer treated mice (P<0.05). However, tumor mRNA expression of inflammatory cytokines, MCP-1, IL-6, and TNF-α, and the macrophage marker, F4/80, did not differ between treatments. Based on the micro array analysis, 206 genes were downregulated with Quer and 69 were upregulated. And a total of 33 pathways were altered with Quer treatment including apoptosis and cytokine signaling. These data provide strong support for a beneficial effect of quercetin on BrCa. These benefits however, at least in this model, are likely due to modulation of inflammatory dependent as well as independent pathways. This work was supported by a COBRE grant from NIH/NIGMS (1P20GM103641-01).
Mugunthan Govindarajan, Ph.D.
Post Doctoral Fellow, University of Arkansas, Fayetteville
weishi@uark.edu

Mugunthan Govindarajan, Ph.D., Lucas Whisenhunt, Wei Shi, University of Arkansas, Fayetteville

OSW-1 is a plant-derived glycosylated steroid (saponin) from Ornithogalum saundersiae bulbs first isolated in 1992. Its mean GI50 against NCI-60 cancer cell lines is 0.78 nM, which is 10–1,000 times more potent than almost all clinically-used anticancer drugs. More intriguingly, OSW-1 showed very promising selectivity (~30-fold) between malignant and nonmalignant cells and can remarkably increase the life span of mice bearing P388 leukemia cells by only one time administration of 0.01 mg/kg. Several biological studies clearly indicated that mitochondria-mediated apoptosis is involved in the cytotoxic effects of OSW-1; however, the first effort to identify target proteins directly interacting with OSW-1 was not reported until 2011. Using affinity chromatography, oxysterol-binding protein (OSBP) and OSBP-related protein 4L (ORP4L) were identified as the major binding partners of OSW-1. Unfortunately, overexpression and knockdown experiments of OSBP or ORP4L only showed moderate (< 6-fold) effects on the potency of OSW-1. The long-term goal of the proposed research is to develop new analogs of OSW-1 for preclinical and clinical evaluations as cancer chemotherapeutic agents. Specifically, we plan to develop an economic and scalable total synthesis of OSW-1. Afterwards, a panel of its derivatives with remarkable structural variations will be synthesized and then evaluated in vitro against cancer cell lines. With the acquired information on structure-activity relationship, we will then design and synthesize fluorescent and affinity probes of OSW-1 to identify its protein targets. Thorough target identification of OSW-1 is critical not only for understanding its modes of action but also to provide essential information that will facilitate future molecular design and medical evaluation of new therapeutic agents derived from it. Herein, the current progress of this project is reported.

Karen H Martin, Ph.D.
Research Associate Professor, West Virginia University
kamartin@hsc.wvu.edu

The Animal Models & Imaging Facility and the Microscope Imaging Facility are two of the shared resources that are supported by the CoBRE for Signal Transduction and Cancer Phase III. These resources are essential for the success of the cancer research program at West Virginia University, and they support a continuum of assays from molecular analysis at the single cell level through pre-clinical small animal models to characterize the signaling pathways that contribute to tumor growth and metastasis. Both facilities are staffed by experienced Imaging Specialists that provide training and assist with experimental design and data analysis. The Microscope Imaging Facility currently has eight microscopes for applications including laser scanning and swept field confocal microscopy, live cell imaging with environmental control, microinjection, TIRF, laser microdissection, color histology records and slide scanning. The Animal Models & Imaging Facility has an IVIS Lumina II optical imaging system for bioluminescence and fluorescence studies in small animal models of cancer. In addition, the facility has a VisualSonics Vevo 2100 system for micro-ultrasound imaging, measurement of 3D tumor volumes and image-guided injections. Both of the in vivo systems provide non-invasive imaging, allowing for longitudinal characterization of disease progression and therapeutic response. The facility also offers additional services including colony management, tumor cell injections, health monitoring, tissue collection, drug administration, surgeries and sperm cryopreservation. This poster highlights some of imaging technologies used in basic and translational cancer research projects with the goal of identifying and characterizing novel targets for therapeutic intervention. The Microscope Imaging Facility and the Animal Models & Imaging Facility have been supported by the Mary Babb Randolph Cancer Center and NIH grants P20 RR016440, P30 RR032138/GM103488, P20 RR016477 and S10 RR026378.
Role of HATx-ERα Complex in ERα-Mediated Transcription in Breast Cancer Cells

Ahmed E. Dhamad
Graduate Student, University of Arkansas
ydu@uark.edu

Ahmed E. Dhamad, Zhenqi Zhou, Ahmed E. Dhamad, Jianhong Zhou, and Yuchun Du University of Arkansas

Transcriptional regulation by estrogen receptor alpha (ERα) is a complex and multistep process, which involves a large number of coactivators and corepressors. In order to identify novel proteins that are involved in ERα-mediated transcription, we used a SILAC (stable isotope labeling by amino acids in cell culture)-based quantitative proteomic method to isolate and identify cellular proteins that interact with ERα. One isoform of histone acetyltransferase, designated as HATx, is one of the identified proteins. We verified the interaction between ERα and HATx with coimmunoprecipitation and established that ERα physically interacts with HATx by performing in-vitro binding assays. Importantly, we found that silencing of HATx by shRNA in breast cancer MCF7 cells resulted in a ~5-fold increase in ERα-mediated transcription in a reporter assay, suggesting endogenous HATx plays an inhibitory role in the ERα-mediated transcription; the shRNA-silencing-induced increase in ERα-mediated transcription was dependent on ERα as the increase in transcription was completely abolished when ERα was silenced by siRNA. Furthermore, we have demonstrated that the purified recombinant HATx blocks binding of purified recombinant ERα to estrogen response elements (EREs) in vitro, suggesting that the inhibitory effect of HATx on ERα transcriptional activity in cells is potentially realized through blocking binding of ERα to the EREs. Lastly, we have demonstrated that silencing of HATx selectively affects the expression of endogenous ERα target genes. Our results suggest that HATx is a novel corepressor of ERα and may play an important role in regulating ERα-mediated gene expression in breast cancer cells.

Non-toxic and stable nano-carriers for delivering an antitumor agent in vivo

Gabriel Barletta, Ph.D.
Professor, University of Puerto Rico - Humacao
gabriel.barletta@upr.edu

Background and Objective: In vivo targeted delivery of the growing number of promising novel short interfering RNA (siRNA)-based therapeutics is an important, but currently challenging, aspect of the drug development process for a variety of diseases, including cancer, viral infections, and autoimmune and neurodegenerative disorders. Our long-term goal is to develop evidence-based clinically-useful drug delivery systems to improve targeted therapies for human disease. Our objective is to develop optimized Super-Paramagnetic Nano Carriers (SPNCs) that can successfully deliver siRNAs to target tissues and to evaluate their pharmacokinetics using an inexpensive in vivo model (Drosophila). The central hypothesis is that SPNCs designed with modified poly(ethylene imines) (PEI) will yield maximal delivery of siRNA molecules to targeted tissues in vivo. Methods: Different SPNC’s were tested in CHO-K1 and HeLa cell lines for their transfection efficiency of firefly luciferase (GL2 + GL3) siRNA and we explored the benefits of magnetofection. Drosophila was successfully used to assess the SPNC’s toxicity and their effects on the flies circadian rhythm. Results: Reducing the polyctionic character of the nanoparticles eases their toxicity while maintaining their high transfection efficiency, which is actually increased by magnetofection. Toxicity results obtained with four additional cell lines highlight that cells tolerate these new nanoparticles differently. The circadian rhythm of Drosophila melanogaster was affected, and a dependence on the SPNC’s surface groups was observed. Discussion and Conclusions: There is a fine balance between the polyctionic character of a carrier to its toxicity and transfection efficiency. Magnetofection is a powerful tool to deliver the carrier-siRNA complex to a target cell or tissue.
Effect of Redox Stabilization on Au(III) Anticancer Agents

Allyn Ontko, Ph.D.
Associate Professor, Arkansas State University
aontko@astate.edu

Allyn Ontko, Ph.D., Kamalakannan Palanichamy, Ohio State University Taylor House, University of Arkansas for Medical Sciences

A series of Au(III) polypyridyl complexes of the general form [AuCl2(polypyridyl)][PF6] (polypyridyl = Dipyrido[3,2-f:2',3'-h]Quinoxaline (DPQ), Dipyrido[3,2-a:2',3'-c] Phenazine (DPPZ) and Dipyrido[3,2-a:2',3'-c][6,7,8,9-tetrahydro] Phenazine (DPQC)) have been prepared and characterized. These complexes have demonstrated significant cytotoxicity in ovarian cancer cell lines but the mechanism of their apoptotic action remains poorly understood. To better elucidate the role of the Au(III) to Au(I) redox couple in anticancer activity, the reduction electrochemistry of these compounds was studied using cyclic voltammetry. The reductive electrochemistry was examined in acetonitrile using tetrabutylammonium hexafluorophosphate as the supporting electrolyte. Multiple reduction waves are observed and the potential of the reduction appears sensitive to the bidentate ligand environment.

Structural activity relationship studies of aza-podophyllotoxin derivatives against ovarian human tumor cell line

Ajay Kumar, Ph.D.
Assistant Professor, School of Environmental Affairs, Universidad Metropolitana
ajkumar@suagm.edu

Ajay Kumar, Vineet Kumar, Sanjay V. Malhotra Laboratory of Synthetic Chemistry, SAIC-Frederick Inc., National Cancer Institute at Frederick, Frederick, MD 21702, USA and Antonio E Alegria Department of Chemistry, University of Puerto Rico at Humacao, Puerto Rico, P.O. Box 860 00792 USA

Etoposide, etopophos and teniposide derived from podophyllotoxin (a natural lignin) and are in clinical use for the treatment ovarian cancer including a variety of malignancies. Etoposide was first synthesised in 1966, and U.S. Food and Drug Administration approval was granted in 1983. Synthesis of podophyllotoxin is not feasible so far and due to this reason structural modification of podophyllotoxin could not be explored very well. The American Cancer Society estimates that in 2013, about 22,240 new cases of ovarian cancer will be diagnosed and 14,030 women will die of ovarian cancer in the United States. According to the data, the mortality rates for ovarian cancer have not improved in forty years since the “War on Cancer” was declared. A woman’s lifetime risk of developing invasive ovarian cancer is 1 in 72. A woman’s lifetime risk of dying from invasive ovarian cancer is 1 in 95. We have developed aza-podophyllotoxin a heterocyclic analogue of podophyllotoxin i.e. N-hydroxyethyl-4-aza-podophyllotoxin derivatives. Some of the new aza-podophyllotoxin derivatives showed promising results against ovarian (OVCAR-5 and OVCAR-3) human cancer cell lines at NCI.
Inhibitors of urokinase type plasminogen activator and cytostatic activity from crude plants extracts

Ezio Fasoli, Ph.D.
Assistant Professor, University of Puerto Rico at Humacao
ezio.fasoli@upr.edu

Ezio Fasoli, Vibha Bansal, University of Puerto Rico at Cayey

Abstract: In view of the clear evidence that urokinase type plasminogen activator (uPA) plays an important role in the processes of tumor cell metastasis, aortic aneurysm, and multiple sclerosis, it has become a target of choice for pharmacological intervention. The goal of this study thus was to determine the presence of inhibitors of uPA in plants known traditionally for their anti-tumor properties. Crude methanol extracts were prepared from the leaves of plants (14) collected from the Subtropical Dry Forest (Guanica) in Puerto Rico, and tested for the presence of inhibitors of uPA using Fibrin Plate Assay. The extracts that tested positive (6) were then partitioned with petroleum ether, chloroform, ethyl acetate and n-butanol, in a serial manner. The resulting partitions were then tested using again the fibrin plate assay. Extract partitions from leaves of Croton lucidus (C. lucidus) showed the presence of a strong uPA inhibitory activity. Serial dilutions of these C. lucidus partitions were performed to determine the uPA inhibition IC50 values. The chloroform partition showed the lowest IC50 value (3.52 µg/mL) and hence the most potent uPA inhibitor. Further investigations revealed that the crude methanol extract and its chloroform and n-butanol partitions did not inhibit significantly the closely related proteases such as the tissue type plasminogen activator (tPA) and plasmin, indicating their selectivity for uPA, and hence superior potential for medicinal use with fewer side effects. In a further evaluation of their therapeutic potential for prevention of cancer metastasis, the C. lucidus extracts displayed cytostatic activity over human pancreatic carcinoma (PaCa-2) cells, as determined through MTS assay. The cytostatic activities recorded for each of the partitions correlated with their relative uPA inhibitory activities. There are no existing reports of uPA inhibitors being present in any of the plants reported in this study.

Targeting the amino acid transporter xCT for the treatment of HIV-associated lymphoma

Zhiqiang Qin, M.D., Ph.D.
Assistant Professor, Louisiana State University Health Sciences Center – New Orleans
zqin@lsuhsc.edu

Zhiqiang Qin, M.D., Ph.D., Lu Dai, Karlie Bonstaff, Chris Parsons (LSUHSC-NO)

The Kaposi's sarcoma-associated herpesvirus (KSHV) is the etiologic agent of several human cancers including primary effusion lymphoma (PEL), which represents a rapidly progressive malignancy arising primarily in patients infected with the human immunodeficiency virus (HIV). Even under conventional chemotherapy, the prognosis for PEL is still very poor, with a median survival time of around 6 months. Therefore, novel targeted strategies are urgently needed for improved treatment. The amino acid transporter, xCT, is essential for the uptake of cystine required for intracellular glutathione (GSH) synthesis and maintaining the intracellular redox balance. Inhibition of xCT functions can induce growth arrest in a variety of cancer cells, although its role in PEL cells remains unclear. Therefore, in the current study, we try to: 1) determine whether inhibition of xCT can cause PEL cell death/apoptosis and understand its potential mechanisms through varied host and viral factors; 2) determine whether xCT inhibitors can reduce PEL progression in an immune-deficient xenograft model. The standard MTT and Annexin V-PI staining were used to assess PEL cell viability and apoptosis. The qRT-PCR, immunoblots, IFA, flow cytometry and other biological and biochemistry assays were used to demonstrate the viral/cellular mechanisms of PEL growth and survival affected by xCT inhibition. A PEL xenograft model in NOD/SCID mice was used to assess the effects of xCT inhibitor in vivo.

We found that xCT was widely expressed on the surface of patient-derived PEL cells, and that reducing xCT expression or function induced significant Caspases-mediated apoptosis for PEL cells. Several potential mechanisms were involved in xCT inhibitors-induced PEL apoptosis, including virus lytic reactivation, repressing cellular signaling pathways and affecting intracellular GSH/ROS levels. Moreover, we found that one xCT inhibitor, Sulfasalazine (SASP), was able to prevent PEL tumor formation in NOD/SCID mice. Our data may lead to innovative mechanistic insights for the role of xCT in HIV-associated lymphoma pathogenesis, and provide the framework for development of xCT-focused therapies and implementation of clinical trials for HIV-infected patients in future.
Identification of Fusarochromanone’s Biological Targets Through Photoaffinity Labeling

Steven Adelmund
Graduate Student, Louisiana State University Shreveport
steven.adelmund@gmail.com

Steven Adelmund, Louisiana State University in Shreveport, Chris Kevil: Louisiana State University Health Science Center in Shreveport; Madison Wynne, Tara Williams-Hart, Brian Salvatore, and Elahe Mahdavian: Louisiana State University in Shreveport

Fusarochromanone (FC101a) is a potential new drug that shows promise in treating a variety of human cancers. FC101a is a mycotoxin, natural product produced by the fungus, Fusarium equiseti. The chemical appears to affect cancer cells differently than other common chemotherapeutic agents. FC101a has demonstrated no innate toxicity to normal cells at lower doses. Despite its discovery in 1985, the mechanism of FC101a’s function remains undetermined. The purpose of this research is to develop an understanding of FC101a’s mode of action using photoaffinity labeling. A photoaffinity label has been synthesized and will be bound to FC101a to facilitate the identification of the biological targets of the drug. UV-irradiation of malignant breast cancer cells treated with labeled FC101a, promotes the formation of a covalent bond between the labeled drug and its biological receptors. Cell homogenate is purified using HPLC followed by proteolytic digestion. The fragments are then sequenced with MS/MS and LC/MS and whole proteins are identified using NCBI’s BLAST. The results of this study will provide insights into the mechanism of FC101a by identifying the protein interactions of the drug in cancer cells. From this, more effective treatment methods can be developed and functional group alterations of FC101a can be proposed that will potentially increase its efficacy.

Development of Recombinant Reovirus as a Therapeutic for Lung Cancer

Emily Simon
Graduate Student, University of Arkansas for Medical Sciences
EJSimon@uams.edu

Emily Simon, Karl W. Boehme, Department of Microbiology and Immunology and Center for Microbial Pathogenesis and Host Inflammatory Response, University of Arkansas for Medical Sciences, Little Rock, AR, 72205

Cancer is the second leading cause of death in the United States. Although great strides have been made in the treatment of many types of cancer, the prognosis for certain malignancies remain poor due to limited treatment options. Clinical trials are underway to determine the efficacy of mammalian orthoreovirus-(reovirus) based oncolytics as cancer therapeutics. The first-generation reovirus-based oncolytic, Reolysin, is safe and selective for cancer cells. Reolysin is a serotype 3 (T3) reovirus that kills cancer cells by inducing apoptosis. However, many cancers develop resistance to apoptosis induced by conventional chemotherapeutics and radiotherapies. Thus, development of cancer treatments that kill cancer cells by alternative mechanisms is of paramount importance. In contrast to T3 reoviruses, serotype 1 (T1) reoviruses kill cells using a non-apoptotic mechanism. It is possible that T1 reoviruses that kill cells by non-apoptotic mechanisms may be more effective cancer therapeutics than apoptosis-inducing T3 reoviruses. Here, we test the capacity of T1 and T3 reoviruses generated by plasmid-based reverse genetics for the capacity to replicate in and kill a panel of lung cancer cell lines. Both serotypes replicated efficiently in each lung cancer cell line tested. Consistent with previous studies, T3 reovirus killed the majority of cell lines. However, some cell lines were resistant to killing by T3 reovirus. T1 reovirus killed each cancer cell line tested, including the cell line that was resistant to the T3 strain. These findings indicate that T1 reoviruses kill lung cancer cell lines as effectively as the T3 virus currently in clinical trials. These studies also suggest that T1 reoviruses can serve as a therapeutic alternative for cancers that are resistant to killing by T3 reovirus.
CN23  Novel Image Markers for Non-small Cell Lung Cancer Classification and Survival Prediction

Hongyuan Wang
Graduate Student, Department of Statistics, University of Kentucky
hongyuan.wang@uky.edu

Hongyuan Wang, Department of Statistics University of Kentucky, Fuyong Xing1,3, Hai Su1,3, Arnold Stromberg2, Lin Yang1,3
Institutions: 1 Division of Biomedical Informatics, Department of Biostatistics, University of Kentucky, Lexington, Kentucky 40536. 2 Department of Statistics, University of Kentucky, Lexington, Kentucky 40506. 3 Department of Computer Science, University of Kentucky, Lexington, Kentucky 40506.

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer and is a serious disease in the world for men and women. Using histopathological image data to automatically and correctly classify two major subtypes, adenocarcinoma (AC) and squamous cell carcinoma (SCC), and to conduct precise survival prediction, is of great importance in providing assistance to diagnosis and personalized therapy planning for the patients. In this paper we propose an integrated framework for NSCLC classification and survival analysis using novel image markers, which includes cell detection, segmentation, classification, and survival analysis. A robust seed detection-based cell segmentation algorithm is proposed to accurately segment each individual cell in the digital slides. Based on cell segmentation results, a set of extensive cellular morphological features are extracted using efficient feature descriptors. A set of most discriminative image markers are selected based on sparse representation to train a support vector machine classifier, which is then used to classify two major subtypes of NSCLC. Finally, a Cox proportional hazards model by component-wise likelihood based boosting is fitted. Significant image markers are accessed using bootstrap analysis and the model’s survival prediction performance is evaluated. The proposed model is applied on the TCGA lung cancer dataset, which has 122 patients’ image with complete clinical information. The classification performance exhibits high correlations between image markers and subtypes of NSCLC while the survival analysis demonstrates strong prediction power of the Cox model using the discovered image markers.

CN24  LC-Morph: A Morphological Image Signature for Predicting Lung Cancer Survival

Yuchen Yang
Graduate Student, Department of Statistics, University of Kentucky
yuchen.y@uky.edu

Yuchen Yang, Fuyong Xing, Division of Biomedical Informatics, Department of Biostatistics, University of Kentucky; Hai Su, Division of Biomedical Informatics, Department of Biostatistics, University of Kentucky; Li Chen, Division of Cancer Biostatistics, Department of Biostatistics, University of Kentucky; Chi Wang, Division of Cancer Biostatistics, Department of Biostatistics, University of Kentucky; Heidi Weiss, Division of Cancer Biostatistics, Department of Biostatistics, University of Kentucky; Janna Neltner, Department of Pathology, University of Kentucky; Craig Horbinski, Department of Pathology, University of Kentucky; Arnold Stromburg, Department of Statistics, University of Kentucky; Lin Yang, Division of Biomedical Informatics, Department of Biostatistics, University of Kentucky

Lung cancer is one of the most common causes of cancer-related death in men and women throughout the world. An appropriate statistical model for survival analysis of lung cancer can provide precise prognosis for treatment planning. Usually the traditional prognostic decisions are made purely based on pathologists’ subjective evaluations. It has been shown that accuracy and objectivity of diagnosis and prognosis, when assisted with a computational algorithm, will dramatically increase. In this paper, we propose an integrated framework of an automatic, high-accuracy, and image-based imaging informatics system (LC-Morph) to predict patient survival risk based on automatically extracted morphological image features. The whole process includes cell detection, segmentation, and building a statistical model for survival analysis. Information on 122 patients extracted from the TCGA data set have been used in this study. A robust seed detection-based cell segmentation algorithm is proposed to accurately segment each individual cell in the image. Based on the cell segmentation results, a set of morphological image features are extracted using some advanced image descriptors. Due to the high dimensionality of the data, L1 regularization cox model is applied to reduce the dimensionality of original data, and the cut off of LC-morph score is chosen by minimizing the area under the ROC curve (AUC). Patients were classified into two groups (low-risk and high risk), and an accurate prediction of survival rate using our discovered image markers was presented. Testing data set was also used to validate the prediction model performance on an independent dataset.
cDNA Microarray Analysis of the Effects of Fusarochromanone in Human Bladder Carcinoma Cells and Budding Yeast

Amber Williams
Graduate Student, Louisiana State University Shreveport
twilliam@lsus.edu

Amber Williams, Phoebe A. Rollyson1, Dominique Washington1, Mickeal N. Key1, Trey C. King1, Jennifer Roberts5, Elahe Mahdavian2, Urska Cvek 3, Marjan Trutschl 3, Brian D. Furmanski4, Yoon-Jee Kim5, Brian A. Salvatore1, Robert E. Rhoads5, and John L. Clifford5
1 Departments of Biological Sciences, 2 Chemistry and Physics, 3 Computer Science, LSU Shreveport, One University Place, Shreveport, LA 71115
4 Siga Technologies, 4575 SW Research Way, Suite 230, Corvallis, OR 97333
5 Department of Biochemistry and Molecular Biology, LSU Health Shreveport, 1501 Kings Highway, Shreveport, LA 71130-3932

Fusarochromanone (FC101) is a toxic metabolite produced by fungi from natural grain or cereal plants. It has been observed to inhibit cell growth in vitro and to reduce tumor growth and increase apoptosis in vivo. FC101 has exhibited the capacity to inhibit cancer growth in a number of human cancer cell lines and may well be a viable consideration for cancer therapy. Identification of those genes that are differentially expressed as a result of treatment with FC101 will lead to detection of the cellular mechanisms that interact with the drug to inhibit the growth of cancer cells. cDNA microarray analysis was performed on human bladder cancer cells and Saccharomyces cerevisiae (budding yeast), which is widely used as a model organism in genetic studies. The analysis revealed a number of orthologous yeast and human genes that, when treated with FC101, exhibit differential expression greater than two-fold. Ingenuity Pathway Analysis revealed that a number of these genes are involved in apoptosis, cell cycle regulation, chromatin remodeling, and ribosomal assembly pathways. RT-qPCR was performed on a select number of these genes to verify the microarray findings. A number of genes that were successfully verified are involved in palmitoylation and/or ubiquitylation. Many genes are involved in histone deacetylation and are directly connected to the regulation of p53 in the DNA repair pathway. These genes represent potential molecular targets by which FC101 inhibits cancer cell growth.

Identification and quantification of plasma membrane proteome of IBC and non-cancerous mammary epithelial cells using SILAC

Ivette Suárez-Arroyo
Graduate Student, Universidad Central del Caribe - School of Medicine
ivettejsuarez@yahoo.com

Ivette Suárez-Arroyo, Juliana Pérez-Laspiur2, Luis A. Cubano1, Suranganie F. Dharmawardhane2, Michelle M. Martínez-Montemayor1
1 Universidad Central del Caribe-School of Medicine, Bayamón, PR, 2 University of Puerto Rico-Medical Sciences Campus, San Juan, PR.

Inflammatory Breast Cancer (IBC) is the most lethal form of breast cancer with a survival rate of <5% in five years. The pathogenesis of IBC was initially defined as an inflammatory reaction. However, the current principle is that the symptoms are associated with the formation of tumor emboli that invade the dermal lymphatics overlying the breast, causing the inflammatory phenotype. IBC cell lines and tumors overexpress plasma membrane (PM) proteins such as E-cadherin and Epidermal Growth Factor Receptor (EGFR), which are associated with maintaining tumor spheroid integrity, increase IBC tumor growth rate, invasion and metastasis. Since more than 50% of all cancer drug targets are PM proteins, and their role in cell-cell interaction and signal transduction is vital for tumor progression in this cancer, it seems essential to define the membrane proteome in IBC. We characterized the PM proteome of two breast cell lines. By culturing non-cancerous mammary epithelial cells (MCF10A) and IBC cells (SUM-149) with light or heavy stable isotopes of amino acids (SILAC), respectively, we have identified and quantified expression of 1,913 membrane proteins by LC/MS. A total of 587 proteins displayed an expression change of 2.5-fold or greater of which 579 were up-regulated in SUM-149 IBC cells and 8 were down-regulated compared to MCF10A cells. This study provides an intriguing insight into the specialized IBC PM with the potential to identify a number of novel therapeutic targets for this intractable disease. This project was sponsored by NIH/NCI #1F31CA174307-01 to ISA, Title V PPOHA US Department of Education #P031M105050 to UCC, NIH/RCMI #5G12RR003035 and #8G12MD007583 to UCC, NIH/RCMI Translational Proteomics Center #2G12RR003051 to UPR-MSC, NIH/INBRE #5P20RR016470 to UPR/UCU and a research donation from the Commonwealth of Puerto Rico to UCC’s University Center of Integral and Complementary Medicine (CUMIC)/MMM.
CN27  Single-step purification of recombinant interleukin-12

Bhanu Prasanth Koppolu  
Graduate Student, University of Arkansas  
bkoppolu@uark.edu

Bhanu Prasanth Koppolu, Srinivas Jayanthi, Sean Smith, T.K.S. Kumar, David A. Zaharoff. Department of Biomedical Engineering,  
Department of Chemistry and Biochemistry, University of Arkansas, Fayetteville, AR

Interleukin-12 (IL-12) is a heterodimeric glycoprotein composed of two disulfide-linked subunits, p35 and p40. Due to its central  
role in cell-mediated immunity, IL-12 has been used, with remarkable success, as an anti-cancer immunotherapy against a  
range of malignancies in preclinical studies. Unfortunately, continued preclinical development of IL-12-based immunotherapies  
has been limited by the exorbitant costs of commercially available recombinant IL-12. The high cost is driven by the complexity  
of the heavily glycosylated heterodimer, the need to use mammalian expression systems and the labor intensive, multi-step  
strategies required to purify recombinant IL-12. We have recently demonstrated that human IL-12 can be purified from high  
expressing HEK293 clones using single-step chromatography. The recovered cytokine was found to be bioactive and >85% pure.  
This novel purification strategy will facilitate future studies of structure-function relationships. Single-step purification will also  
provide sufficient quantities of recombinant IL-12 as well as IL-12 analogs for preclinical immunotherapy studies.

CN28  Structure-activity relation of D-aminoacid containing peptidomimetics for inhibition of protein-protein  
interactions of EGFRs

Shanthi Kanthala  
Graduate Student, University of Louisiana at Monroe  
kanthasp@warhawks.ulm.edu

Shanthi Kanthala, Ted Gauthier, Seetharama D. Satyanarayanajois

HER-2 (Human Epidermal growth factor Receptor 2), a member of EGFR (Epidermal Growth Factor Receptor) family is normally  
involved in the signal transduction pathways leading to cell growth and differentiation. Overexpression of HER2 and  
deregulation of signaling has implications in breast, ovarian and lung cancer. We have designed several peptidomimetics to  
block the HER2 mediated dimerization resulting in antiproliferative activity for cancer cells. Earlier, a peptidomimetic compound  
S, designed based on the crystal structure of HER-2 and Trastuzumab has been reported to have antiproliferative activity in the  
nanomolar range. In the present work we have investigated the structure-activity relationship of peptidomimetic analogs of  
compound S. Compound S was conformationally constrained by N- and C-terminal modification and cyclization as well as  
substitution with D-amino acids at N-and C-termini. Among the compounds studied in this work, a peptidomimetic compound  
21 with D-amino acid substitution with its N- and C-termini capped with acetyl and amide functional group and reversed  
sequence in comparison with compound 5 exhibited better antiproliferative activity in HER2 overexpressed breast, ovarian and  
lung cancer cell lines. The compound 21 was further evaluated for its protein-protein interaction inhibition ability using  
pathhunter assay and western blot analysis. Results suggested that compound 21 is able to block HER2: HER3 interaction and  
inhibits phosphorylation of kinase domain of HER2.  
This project was supported by the National Institutes of Health through the National Institute of General Medical Sciences Grant 8P20GM103424 via Louisiana Biomedical Research Network (LBRN).
CN29  Isoform-specific roles for Akt1 and Akt2 in the invasiveness of pancreatic cancer

Pooja Ghai
Graduate Student, Arkansas State University
gzhou@astate.edu

Pooja Ghai, Pooja Ghai1,2, Huhehasi Wu1, Haitao Zhang1,2 & Guo-Lei Zhou1,2  1. Department of Biological Sciences, Arkansas State University, State University, AR 72467  2. Molecular Biosciences Program, Arkansas State University, State University, AR 72467

Pancreatic cancer has the worst prognosis among cancers with a 5-year survival rate at ~4%. The main reason behind the dismal outcome is the frequent metastasis due to the highly invasive property of the disease as well as difficulties in early detection. Developing therapeutic targets and/or biomarkers for controlling pancreatic cancer metastasis is the key for improving the outcomes. Akt has been implicated in stimulating metastasis in a variety of human cancers, and targeting the PI-3kinase/Akt signaling pathway has been widely pursued for cancer treatment. Previous studies, including our own, have shown opposing roles for Akt1 and Akt2 in the motility of both fibroblasts and breast cancer cells, although the exact roles appear to be cell context-dependent. Akt2 has been shown to be up-regulated in pancreatic cancer, suggesting that it may stimulate cancer metastasis. The main goals of this project are to dissect roles of Akt1 and Akt2 in the motility and invasion of pancreatic cancer cells. Using RNAi strategy, we silenced Akt1 and Akt2 in PANC-1 and MIA PaCa-2 cancer cells. We found that Akt1 knockdown (KD) significantly increased cell motility while Akt2 KD also modestly increased motility. We also found that depletion of Akt1 and Akt2 caused distinct alterations in the actin cytoskeleton. Akt1 KD cells had enhanced and more organized stress fibers while Akt2 KD cells had remarkably reduced stress fibers. Both Akt1 KD and Akt2 KD cells were larger than the cells harboring empty vector, and Akt2 KD cells were also larger than Akt1 KD cells. Akt2 KD cells also had increased cell proliferation rate than the Akt1 KD and control cells. Insights into the isoform-specific roles for Akt in pancreatic cancer could open up avenues for more effective strategies for inhibiting Akt in pancreatic cancer treatment, such as developing isoform-specific Akt inhibitors that are more effective and meanwhile with reduced side/adverse effects.

CN30  Exploring the role of the actin regulatory protein CAP1 in the motility and invasion of breast cancer cells

Haitao Zhang
Graduate Student, Arkansas State University
gzhou@astate.edu

Haitao Zhang, Haitao Zhang1,2, Pooja Ghai1,2, Huhehasi Wu1 & Guo-Lei Zhou1,2  1. Department of Biological Sciences, Arkansas State University, State University, AR 72467  2. Molecular Biosciences Program, Arkansas State University, State University, AR 72467

Deregulation of the actin cytoskeleton underlies pathological conditions including metastasis of cancer. Cyclase-associated Protein 1 (CAP1) is a key actin regulatory protein that facilitates cofilin-driven actin dynamics, and emerging evidence, mostly derived from preliminary gene profiling studies, also suggests a role for deregulated CAP1 in cancer invasiveness. In mammalian cells such as fibroblasts, knockdown of CAP1 reduces cell motility because of reduced actin dynamics. However, in HeLa cells, knockdown of CAP1 actually led to increased cell motility and invasion due to activation of adhesion signaling. We aimed to determine the role of CAP1 in breast cancer cell motility and invasion. We first compared CAP1 expression and found no significant up-regulation of CAP1 in the invasive breast cancer cell lines MDA-MB-231 (adenocarcinoma) and BT-549 (ductal cancer) compared to non-invasive cancer cell line MCF-7 and normal breast epithelial cell line MCF-10A, although CAP1 expression appears to be dynamically regulated. We next generated stable cells with efficient CAP1 knockdown, and found that CAP1-depletion in MDA-MB-231 and BT-549 cells led to substantially increased cell motility and invasion. In contrast, knockdown of CAP1 in MCF-10A cells did not affect cell motility. CAP1 knockdown BT-549 cells were larger with a more rounded shape and Phalloidin staining revealed large, fan-like lamellipodia as well as developed actin arcs in lamella area; these phenotypes are known to drive cell motility. Vinculin staining in these cells showed increased numbers, but reduced size, of focal adhesions, and we also found significantly elevated FAK (Focal Adhesion Kinase) activity in these cells. Taken together, our results indicate that knockdown of CAP1 actually promoted breast cancer cell motility and invasion, suggesting that CAP1 might function to suppress the invasiveness of breast cancer.
Cofactor Genomics: Providing Next-Gen Sequencing support to IDeA and INBRE researchers

Natalie A. LaFranzo, Ph.D.
Project Scientist, Cofactor Genomics
natalie_lafranzo@cofactorgenomics.com

Natalie A. LaFranzo, Joshua C. Ferrell, James A. Bradley, Janelle M. Hare, Morehead State University

The ability to generate hundreds of gigabases of data has made next-generation sequencing (NGS) an indispensable technique for interrogating complex biological questions. Cofactor Genomics, a leading contract research organization, provides researchers with access to the knowledge and tools to make use of next-generation sequencing within the context of their own research projects. Offering a front-to-back service, Cofactor provides support from experimental design through molecular techniques and bioinformatics analysis.

By partnering with the Kentucky IDeA Network of Biomedical Research Excellence (INBRE) program, Cofactor has supported INBRE researchers seeking to use NGS to demonstrate feasibility and preliminary results, with the goal of securing larger funding opportunities. One example of such a partnership is with Dr. Janelle Hare, an INBRE PI at Morehead State University. Working with Dr. Hare, Cofactor provided experimental design, sequencing, and analysis support to investigate the SOS response to DNA damage. This project utilized RNA-sequencing to analyze the Acinetobacter baylyi ADP1 DNA-damaged transcriptome. This environmental microbe’s transcriptome was compared to that of the opportunistic pathogen, Acinetobacter baumannii, to examine whether the gene set induced in these different species is highly conserved within the genus.

Other applications of NGS that are amenable to INBRE projects include de novo assembly of novel organisms, and single-nucleotide polymorphism (SNP) detection. With all applications, researchers obtain actionable results that they have confidence in for publication and grant applications. Furthermore, Cofactor provides educational and training opportunities to the institutions and researchers within the INBRE program.

Spectroscopic Analysis of Fusarochromanone: A Potential Anti-Cancer Agent

Peyton Rachal
Undergraduate Student, Louisiana State University Shreveport
peytonrachal@gmail.com

Peyton Rachal, Phillip Palyok, Brian Salvatore, and Elahe Mahdavian

Fusarochromanone (FC101a) is a potential anti-angiogenic and anti-cancer agent that has shown promise in vitro but has some complications in vivo. The purpose of this project is to gain a better understanding of the physical and chemical properties of FC101a in order to proceed with further structure-based drug development. The protocol for determining the spectra was developed using Kynurenine (a structural analog of FC101a) and 6-hydroxy-2,2-dimethyl 4-chromanoneone (a compound with a similar core chromanone group to FC101a). The experimentation consisted of finding a proper solvent and gathering the spectroscopic data at pHs 1 – 13. With this protocol developed, the Uv-Vis spectroscopic data for FC101a was elucidated, and that data will lead to being able to better understand its chemical and biological effects and help in further drug design.
Analysis of the Apoptotic Effects of Fusarochromanone using Western Blotting and Fluorescence Assay

Phillip Palyok
Undergraduate Student, Louisiana State University in Shreveport
palyokp68@lsus.edu

Phillip Palyok, Ying Gu (LSUHSC-S), Madison Wynn, Peyton Rachal, Shile Huang (LSUHSC-S), Tara Williams-Hart, Brian Salvatore, and Elahe Mahdavian

Fusarochromanone (FC101) is a small molecule mycotoxin that is produced by the fungus Fusarium equiseti. Recent studies have shown that FC101 is a potent anticancer agent, by inducing programmed cell death (apoptosis) and inhibiting angiogenesis. The purpose of this project is to investigate the molecular mechanism by which FC101 induces apoptosis in human breast cancer (MDA-MB-231) cells. Apoptosis can be induced by caspase-dependent and/or -independent mechanism.

In this study, MDA-MB-231 cells were treated with FC101, followed by MTS assay, western blotting, and caspase fluorescence assay. We found that treatment with FC101 for 72 h reduced the cell viability in a concentration-dependent manner, with an IC50 = 500 nM. Furthermore, exposure to FC101 (0-1000 nM) for 24 h dose-dependently elevated caspase-3/7 activity in the cells, and also increased cleavage of PARP, a well-known substrate of activated caspases and a hallmark of caspase-dependent apoptosis. However, to our surprise, FC101 did not affect expression of anti-apoptotic (Bcl-2, Bcl-XL, Mcl-1) or pro-apoptotic proteins (BAD, BAK, BAX). Therefore, FC101-induced apoptosis is caspase-dependent, but may not be through an intrinsic mechanism. Future experiments will investigate whether FC101 affects the activity of caspase-8 and the expression of death-receptor signaling proteins (TNF-α, TRAIL, FasL, TNFR, and FAS/CD95) to further confirm that FC101 induction of apoptosis is death receptor mediated through an extrinsic pathway.

Optimization of Gold Nanoshell-Mediated Photothermolysis of Lymphatic Endothelial Cells

Israel Soto
Undergraduate Student, Louisiana State University Shreveport
sotoi72@lsus.edu

Israel Soto, Kui Chen - LSU Shreveport W. Todd Monroe - LSU Baton Rouge J. Steven Alexander - LSUHSC Shreveport

Recent studies suggested that tumor-associated lymphatics play important roles in tumor growth and metastasis. In this project, gold nanoshell (AuNS)-mediated photothermolysis targeting the lymphatic vessels is investigated as a strategy to inhibit tumor metastasis through the lymphatics. AuNSs are optically tunable nanoparticles that absorbs strongly in the near-Infrared and capable of efficiently converting absorbed light into heat when irradiated with light of appropriate wavelength. These properties can be used to induce photothermal injury to lymphatic endothelial cells (LECs) and disrupt lymphatic vessels.

The main goal in this study is to optimize the AuNS-mediated photothermolysis of the LECs. First, the time-dependent AuNS uptake by the LECs was examined. Results showed that more AuNSs were taken up by the LECs with longer incubation time. Power density of the laser irradiation was found to be critical for effective photothermolysis of LECs using AuNS. Higher power density was achieved by increasing the laser power and focusing the beam. With sufficient power density, the effectiveness of AuNS-mediated photothermolysis increases with both AuNS concentration and irradiation time. To enhance AuNS update by the LECs and improve the specificity of AuNS-mediated photothermolysis, anti-VEGFR3 antibody is introduced onto the AuNS surface via a polyethylene glycol linker. This will allow the modified AuNS to actively target LECs, which over-express VEGFR3 on the cell membrane.
CN35 Biological function of parathyroid hormone related protein fragment 12-48 (PTHrP 12-48)

Julianna Grillot
Undergraduate Student, University of Arkansas
jgrillot@uark.edu

Breast cancer treatment and diagnosis is complicated by the metastasis of malignant tumor cells to bone tissue commonly seen in breast cancer patients. The prediction and early detection of metastatic breast cancer cells is critical, yet extremely difficult due to a lack of viable and reliable biomarkers. Recently, our lab discovered a parathyroid hormone related protein 12-48 (PTHrP 12-48) as a potential biomarker of breast cancer bone metastasis in the serum of patients. Our previous studies demonstrated that parathyroid hormone related protein (12-48) (PTHrP(12-48)) is a predictive biomarker of breast cancer bone metastasis. In an effort to ascertain whether parathyroid hormone related protein fragment 12-48 has any bioactivity at the cognate parathyroid hormone receptor 1 (PTH1), PTHrP(12-48) was synthesized for biologic characterization in human SaOs2 cells that express the PTH1 receptor and was used as an immunogen. SaOs-2 cells were treated with PTHrP(12-48) and c-AMP accumulation was measured. There was no significant increase in c-AMP accumulation observed, although the cells did respond to PTH(1-34). In addition, no effects of PTHrP(12-48) were observed in osteoblast and adipocyte differentiation experiments. In addition, immunostaining of matched primary tumor and bone metastatic tissue from breast cancer bone metastasis patients demonstrated the expression of PTHrP(12-48) in both bone metastasis and primary tumors, with no detectable staining in normal breast ducts. Interestingly, an inhibitory effect of PTHrP(12-48) on SaOs-2 proliferation by PTHrP(12-48) was observed. Further studies are being performed using PTHrP(12-48) to determine how PTHrP(12-48) is taken up into human cells.

CN36 Investigation of Genome Instability Due to Mutations in the SAM1 and SAM2 Genes and Checkpoint-Deficiencies

Justin T. Gibson
Undergraduate Student, Northern Kentucky University
gibsonj11@mymail.nku.edu

Previous research by our group has identified a set of genes in Saccharomyces cerevisiae, which when heterozygously mutated show increased genome instability effects dependent on secondary checkpoint deficiency. The goal of this project is to explore the role of particular mutations, in the SAM1 and SAM2 genes, in the formation of cells that are genomically unstable, a phenotype often seen in cancer. SAM1 encodes for an enzyme that catalyzes the formation of S-adenosyl methionine (AdoMet) from methionine and ATP. AdoMet is conserved in human cells where changes in its concentration have been implicated in genome instability. We first sought to measure the dosage effects of mutations in this gene on genome stability using two different phenotypic assays, colorimetric sectoring due to loss of a chromosome fragment and whole chromosome V loss measured by fluctuation analysis. These tests confirmed that heterozygous mutations of sam1Δ /SAM1 result in a significant increase in genome instability in a rad9-deficient background. Current studies are aimed at determining if this increase is specific to rad9-deficiency or if they are recapitulated in other checkpoint-deficient backgrounds. We have further noted that the phenotype of increased instability is only seen due to haploinsufficiency of SAM1, while homozygous deletion restores stability. This result will be further investigated by study of mutations in a second gene encoding the enzyme S-adenosylmethionine synthetase, known as SAM2.
Impact of mutations in branched-chain amino acid availability genes on genome stability in Saccharomyces cerevisiae

Gabrielle Rexy I. Sevilla
Undergraduate Student, Northern Kentucky University
sevillag1@mymail.nku.edu

Previous studies designed to detect haploinsufficiency impacting genome stability in the yeast Saccharomyces cerevisiae identified mutations in genes involved in branched-chain amino acid availability. We hypothesize that availability of these amino acids may impact protein synthesis as well as nutrient-sensing pathways involved in cell cycle progression. In these studies we aim to characterize the full spectrum of genes in this biosynthesis and transport pathway that result in increases in chromosome loss when mutated. To begin research with these genes, heterozygous mutations were made by substituting the genes with a selectable marker deletion cassette. Instability assays were then utilized; the first tests for genomic instability via a colorimetric assay that measures the loss of a chromosome fragment from the cell, the second assays for whole chromosome V loss via fluctuation analysis. In addition to characterizing impacts due to gene mutations we are also interested in genome stability fluctuations due to alteration in branched-chain amino acids concentrations in the growth media. Future directions for this project are to investigate the dosage sensitivity of interesting mutations and determine the mechanism of action in the strains that show increased instability.

Restoring Apoptotic Activity in a Small Cell Lung Cancer cell Line through Inhibition of IGF-1 Signaling

Tyana D. McNeill
Undergraduate Student, South Carolina State University
gwarsham@scsu.edu

Small Cell Lung Cancer (SCLC) is the most aggressive and lethal subtype of lung cancer. The Insulin-Like Growth Factor I (IGF-1) pathway plays an important role in SCLC. We investigated the potential of targeting the IGF-1 receptor, (IGF-1R) and mammalian target of rapamycin (mTOR), a kinase that is activated by the PI3/Akt pathway, as a potential therapeutic strategy against SCLC. H526, a SCLC cell line was used to monitor cell growth and cell signaling activity after the treatment of the cells with NVP-ADW 742 (NVP), an inhibitor of the kinase domain of IGF-1R, and RAD001 (Everolimus, EVE), an inhibitor of mTOR, which is used in anti cancer treatments in advanced renal cell carcinoma and other malignancies; evidence show that RAD001 induced apoptosis is prevented by IGF-1. In the current investigation, concurrent inhibition of IGF-1R and mTOR is used to restore induction of apoptosis in H526 cells. To establish optimal inhibitor concentrations, MTT cell growth assays were performed with various concentrations of the drugs individually and in combination. Currently Western Analysis is being carried out to monitor the by-products of the apoptotic process after treatment of the cells with NVP and EVE to determine if apoptosis is induced by the treatments. (Supported by SC INBRE)
CN39  Effect of Cis/Trans Ligand Environment on Au(III) Anticancer Activity

Jared Burks  Undergraduate Student, Arkansas State University
aontko@astate.edu

Jared Burks, Kamalakannan Palanichamy; Ohio State University Allyn Ontko; Arkansas State University

It is well established that optimal anticancer activity of platinum-based agents, such as cisplatin or oxaliplatin, relies on a cis-configuration of nitrogen-containing ligands about the central atom. Interestingly, platinum agents with ligands that are oriented in a trans- fashion display little to no anticancer activity. We undertook to determine if a cis ligand configuration similarly affects the anticancer activity of Au (III) complexes. To this end, the complex we will call “cis-Au (III)” ([Au(bpy)Cl2]Cl) and the complex we will refer to as “ trans-Au (III)”, ([trans-Au(pyr)2Cl2]PF6) were synthesized and analyzed for anticancer activity in cisplatin sensitive and cisplatin-resistant ovarian cancer cells through cell death studies. We will describe the synthesis of these compounds, their relative anticancer activities in both lines, and any supporting studies which describe the anticancer action of these agents.

CN40  Breast Cancer Prevention: Process of Data Input and Tracking At-Risk Communities

Raven Gray and JaQualane Scales  Undergraduate Student, University of Arkansas for Medical Sciences
njgreerwilliams@uams.edu

Raven Gray and JaQualane Scales, Kimberly S. Enoch, Dr. Nancy Greer-Williams and Dr. Thomas Kieber-Emmons, UAMS

The Mobile Mammography Program (MMP) of Arkansas was initiated to address the lack of mammography facilities in the State. At the inception of the program Arkansas in 2001, 23 of Arkansas’ 75 counties were without mammography facilities. To date there remain no permanent certified mammography facilities in 25 counties, which continues to pose a major dilemma in women obtaining mammograms. The MMP works with primary care providers and local health units to establish sites for screening in the 25 counties that lack FDA-approved certified mammography facilities. The MMP serves as a referral system to educate, navigate and refer women to breast care services and increase screening in each public health region. This permits the MMP to screen cost-effectively and aid in recruitment and enrollment for the Arkansas Department of Health (ADH) BreastCare program for those women who do not receive services. The Winthrop P. Rockefeller Cancer Institute tracks the MMP navigational patient data from the intake and referral forms. This poster outlines the data collection efforts of four undergraduate students which will eventually be constructed into a website to meet the needs of the Arkansas Department of Health and the University of Arkansas for Medical Sciences Cancer Control Program.

CN41  Breast Cancer Prevention: Improving Mobile Mammography Access to Rural At-Risk Communities

Nicole S. McGehee and Jacqueline D. Eldridge  Undergraduate Students, University of Arkansas for Medical Sciences
njgreerwilliams@uams.edu

Nicole S. McGehee and Jacqueline D. Eldridge, Kimberly S. Enoch, Dr. Nancy Greer-Williams and Dr. Thomas Kieber-Emmons, University of Arkansas for Medical Sciences

According to the 2006 Medicaid HEDIS report, there is a significant disparity in breast cancer screening rates among rural and underserved populations, especially African Americans. Despite major screening programs and public awareness, only one third of eligible women in the United States (US) have received screening mammograms over the last 16 years. Barriers such as financial and time constraints, cultural taboos and lack of awareness have been identified as deterrents toward mass screenings. Along the Delta region of the state, the rates are less than 30.5%. The paucity of mammography facilities couples with increased distance needed to travel to obtain a mammogram also amplifies non-compliance with screening recommendations. Mammography is the best method available to detect breast cancer in its earliest stages, when the disease is most treatable. Mobile mammography units reach approximately 12-16% of the at-risk population of women in counties that lack a stationary mammography unit. This research outlines how undergraduate students worked as patient navigators in the University of Arkansas for Medical Sciences Winthrop P. Rockefeller Cancer Institute to reduce cancer health disparities in the state of Arkansas. The overall goal of the proposed Modular Mammography Program—to significantly improve access to and utilization of beneficial cancer interventions in communities with cancer related health disparities.
HCMV-mediated dysregulation of epigenetic pathways in persistently-infected colon cancer cells

Julia Tobacyk
Undergraduate Student, Louisiana Tech University- Ruston, LA
julia.tobacyk@gmail.com

Julia Tobacyk, Shannan Washington and Dr. Donna Neumann (LSUHSC- New Orleans, Dept. of Pharmacology and Therapeutics)

Human cytomegalovirus (HCMV) is a ubiquitous herpes virus that persistently infects 50-90% of adults in the USA. For most healthy people, HCMV is asymptomatic but in immunocompromised individuals including recipients of organ transplants and AIDS patients, it may cause severe and often fatal diseases. Recent findings suggest a close link between cancers and HCMV in which the viral DNA is claimed to have oncomodulatory properties. Oncomodulation means that HCMV infects tumor cells and increases their malignancy. In this study, we explore the epigenetic pathways that are linked to cancer. Our main focuses are two proteins, EXH2 and c-myc, which both show an overexpression in colon cancer cells infected with HCMV. EZH2, HCMV, and c-myc expressions were determined by Western blots in both mock-infected and HCMV-infected colon tumor cells. HCMV, as well as overexpression of EZH2 and c-myc, was detected in colon cancer cells persistently infected with HCMV and, importantly, in healthy tissue there was no expression of EZH2 or c-myc. EZH2 and c-myc were overexpressed in colon tumor cells relative to normal colon cells. Also, colon tumor cells persistently infected with HCMV show a significantly larger overexpression of EZH2 and c-myc compared to uninfected colon tumor cells. Overexpression of both proteins leads to dysregulation of epigenetic mechanisms which are linked to a number of tumors, including those of the colon.

Evaluating the Reliability of the ARTQ in Assessing Cancer Clinical Trial Perceptions in a Predominantly Black Sample in SC

Franshawn Mack
Undergraduate Student, South Carolina State University
franshawn94@yahoo.com

Franshawn Mack, Dr. Marvella Ford Ms. Dana Burshell Mr. Wei Wei Dr. Elizabeth Garrett-Mayer Medical University of South Carolina

Background: African-Americans (AAs) are disproportionately affected by cancer mortality compared to their European American (EAs) counterparts. While greater participation in cancer clinical trials among AAs could help reduce this disparity, negative trial perceptions could negatively impact trial participation. Objective: To evaluate the reliability of the Attitudes towards Randomized Trial Questionnaire (ARTQ) in assessing perceptions of cancer clinical in predominantly African American populations in South Carolina. Methods: Principal Component Analysis and Cronbach’s alpha estimates were used to assess the reliability of the ARTQ in a convenience sample of 315 participants (81.4% AA), from 2008 to 2013, who lived in South Carolina counties with high racial disparities in cancer mortality rates. Results: Slightly more than half of the participants had at least a college diploma (60.8%), 84.8 % were female, and 53.4 % had an annual income of $40,000+. In this study, Cronbach’s alpha was shown to be 0.86. Conclusion: The ARTQ displayed strong evidence of high statistical reliability. This analysis has great implications for future research because it represents the first test of reliability of the ARTQ in a predominantly African American sample and lays the groundwork for use of the ARTQ in future studies in diverse populations.
Using Spheroids and a Bioluminescent Mouse Model to Determine the Effects of Ajulemic Acid on Ewing’s Sarcoma

Drake Hardy
Undergraduate Student, Ouachita Baptist University, Arkansas
har50046@obu.edu

Drake Hardy, Amy Eubanks1, Joseph Levy2, Nathan Koonce2, Rob Griffin2, Lori Hensley1  1 Ouachita Baptist University, Department of Biology 2 University of Arkansas for Medical Sciences, Department of Radiation Oncology

Ewing’s Sarcoma is a pediatric bone cancer with a five-year survival rate of only 30%. New treatment options for this highly aggressive disease are desperately needed. Ajulemic acid (AJA), a synthetic cannabinoid, has been the focus of our research, which has shown that AJA decreases cell viability, and inhibits endothelial cell migration and angiogenesis. Based on these results, AJA is a potential therapeutic agent for Ewing’s Sarcoma and other solid pediatric cancers. In order to create a realistic environment in vitro in which to study these tumors, we are creating 3-dimensional spheroids with three cell types, each of which fluoresces a different color. These include: fibroblasts, which give the spheroids a connective tissue component, endothelial cells, and cancer cells. These spheroids will then be treated with different concentrations of AJA and compared to control groups in an effort to understand cellular proteins or pathways being modulated by our drug. Also, in order to test AJA in a more realistic model of human cancer, we developed a novel bioluminescent mouse model of Ewing’s Sarcoma. We are currently comparing luminescent to physical measurements and assessing the ability of AJA to decrease tumor growth in vivo. It is our hope that our findings will show support for AJA as a potential new cancer treatment option.

Cardiovascular Research

Identifying Potential R/S-Warfarin Metabolite Biomarkers to Improve Anticoagulant Dosing Strategies in Children

Dakota Pouncey
Undergraduate Student, Hendrix College
Pounceydl@gmail.com

Dakota Pouncey, C. Preston Pugh2, Drew R. Jones2, Gunnar Boysen3, Kathleen Neville4, and Grover P. Miller2  2 Department of Biochemistry and Molecular Biology, University of Arkansas for Medical Sciences, Little Rock, AR 3 College of Public Health, University of Arkansas for Medical Sciences, Little Rock, AR 4 Children’s Mercy Hospital, Kansas City, MO

Coumadin (R/S-warfarin) is an anticoagulant drug marketed globally to manage thromboembolic events. Warfarin therapy is very effective, but remains challenging as a result of a narrow therapeutic range and high inter-individual variations in response to treatment. While most warfarin therapy data corresponds to adults, optimal pediatric dosing is significantly different and further complicates treatment in children. Therefore, it is critical to develop ways to improve pediatric warfarin therapy. We hypothesize that metabolite profiles in plasma can be used to predict a safe and effective warfarin therapy based on the results of a single blood test. In a preliminary study, we determined metabolite profiles of R/S-warfarin metabolites for eight pediatric patient plasma samples through the University of Arkansas for Medical Sciences Metabolomics Core Facility. The patient medical histories were analyzed to determine three clinical outcomes of each individual: (1) time to achieve stable therapeutic response; (2) warfarin dosage to maintain stable therapeutic response; and (3) percent time out of therapeutic response. We then employed a simple Pearson correlation analysis to identify correlations among metabolic pathways to better understand the underlying mechanisms of warfarin metabolism. Secondly, we identified correlations between metabolic pathways and clinical outcomes to identify metabolite biomarkers that could be used to predict patient response. Correlations between metabolites offered insight into the enzymatic pathways responsible for their formation and correlations between metabolites and clinical outcomes identified potential biomarkers of adverse outcomes. We also found that changes in CYP2C9 activity may be compensated by CYP3A4, possibly influencing warfarin dosing and drug-drug interactions. A larger sample set in future studies will reveal more reliable predictors of patient dose responses to warfarin therapy.
CV06  Simple and rapid simultaneous measurement of potassium in plasma and red blood cells as a biochemical marker for hypertension

Kebede Gemene, Ph.D.
Assistant Professor, Northern Kentucky University
gemenek1@nku.edu

Kebede Gemene, (1) Jacob Shaffer, Northern Kentucky University; (2) Alinaloana Dogar, Babes-Bolyai University, Cluj-Napoca, Romania; (3) Benjamin Stevens, Northern Kentucky University

Hypertension is a cardiovascular disease, which is among the leading causes of death in the U.S. Thus, assessment of the risk, development and treatment of hypertension is critically important for health care applications. Recent studies have shown that in addition to plasma potassium, red blood cell potassium (RBC-K) can be an important biochemical marker for hypertension, where hypertensives and their offspring were found to have significantly lower RBC-K.1 Therefore, simple, accurate and sensitive measurement of potassium in plasma and RBCs is very important for early detection of hypertension. Nowadays, potentiometry is routinely used for clinical analysis of blood electrolytes in plasma. In fact, today, over 99% of clinical laboratories use classical potentiometry for the analysis of potassium in plasma. However, although it is very convenient for plasma potassium measurement, classical potentiometry cannot directly measure RBC-K. Release of RBC-K by lysis and then detection by classical potentiometry is possible2 but requires continuous pre-calibrations of electrodes. This consume sample and more importantly time. We report here pulsed chronopotentiometry, as a simple, inexpensive and fast method for simultaneous measurement of potassium in plasma and RBCs. Here, a controlled current pulse is applied across a potassium ion selective membrane to cause extraction of potassium from the sample into the membrane. This causes depletion of the ions locally at the membrane surface on the sample side at a given time called transition time. This transition time is a function of concentration according to the well-known Sand Equation. Thus, the concentration of potassium is easily determined from the observed transition time, which is obtained from inflection point on the potential-time curve (chronopotentiogram).


CV07  Radiofrequency Renal Nerve Ablation Attenuates Hypertension in Spontaneously Hypertensive Rats (SHR)

Daniel R. Kapusta, Ph.D.
Professor, Louisiana State University Health Science Center
dkapus@lsuhsc.edu

Daniel R. Kapusta, Ph.D., Juan Gao, M.D., Department of Pharmacology, LSUHSC, New Orleans, LA

Radiofrequency catheter ablation (RF-ABL) of the renal arteries decreases blood pressure (BP) in patients with drug-resistant hypertension. This study investigated whether RF-ABL of the renal arteries alters BP in spontaneously hypertensive rats (SHR). Methods Nineteen-week old male SHR were instrumented with radio-telemetry probes for chronic measurement of BP (Systolic, SBP; Diastolic, DBP). After 1-week, control BP was measured in rats for 3 days. The next day SHR were anesthetized and randomly received either bilateral Sham-ABL (n=5) or RF-ABL (n=6) of the renal arteries (Biosense Webster Stockert 70 generator and RF-probe). The tip of the RF-probe was applied externally to a small dissected segment of each renal artery and stimulated circumferentially. BP was then measured three times a week for 8 weeks. Results In anesthetized hypertensive SHR, RF-ABL of a single renal artery did not alter BP. In contrast, subsequent RF-ABL of the contralateral renal artery produced an immediate (<15 seconds) decrease in mean arterial blood pressure (MAP, range Δ -60 to -100 mmHg). BP in hypertensive SHR was not altered during or after the Sham-AB procedure. In conscious SHR, BP was significantly decreased the day after RF-ABL (153±8/102±4 mmHg) and throughout the post-ABL study (4-week SBP/DBP, 173±7/120±5; 8-weeks, 171±6/116±4 mmHg) compared to pre-ABL control levels (SBP/DBP, 187±9/130±5 mmHg). At the end of week-1 the peak increase in MAP to cage switch stress was significantly blunted and the time to return to basal BP was shortened in RF-ABL. At the end of week-8, the hypotensive response to i.p. chlorisondamine was blunted in RF-ABL rats. Conclusions These data demonstrate that in hypertensive SHR, bilateral RF-ABL of the renal arteries produces a reduction in BP presumably via blockade of renal sympathetic afferent/efferent neural pathways. Funding provided by Biosense Webster (IIS-175).
CV08 Isolation of a natural Nrf2 activator from American ginseng

Taixing Cui, Ph.D.
Assistant Professor, University of South Carolina
bin.li@uscmed.sc.edu; leedonggonk@sina.com

Bin Li1, Akram Abdalrahman1, Yimu Lai1, Lei Shao1, Hechu Li1, Bryan J. Mathis1, Anthony Windust2, Lorne J. Hofseth3, Joseph J. Janicki1, Mitzi Nagarkatti4, Dongqi Tang1, Taixing Cui1 1Department of Cell Biology and Anatomy, 4Department of Pathology, Microbiology and Immunology, University of South Carolina School of Medicine, Columbia, SC 29208, USA 2Measurement Science and Standards, National Research Council, Ottawa, ON, Canada K1A 0R6 3Department of Pharmaceutical and Biomedical Sciences, South Carolina College of Pharmacy, University of South Carolina and Medical University of South Carolina, Columbia, SC 29208, USA

Nuclear factor erythroid-2 related factor 2 (Nrf2), a major transcription factor of the endogenous antioxidant defense system, has been proposed as a potential therapeutic target for the treatment of various diseases. It is likely that Nrf2 signaling is cell type specific and the biological consequences are largely linked to Nrf2 activators. However, a small molecule-driven Nrf2 signaling therapeutic approach remains to be established. Herein, we report one such possibility discovered by the bioassay-based fractionization of American ginseng, an edible folk medicine that has been used for thousands of years in Asia. Since crude extract of American ginseng was found to suppress the expression of inducible nitric oxide synthase (iNOS) in lipopolysaccharide (LPS)-inflamed macrophages via activating Nrf2, we further fractioned the crude extract using solvents including hexane, dichloromethane, ethyl acetate, butanol, and water, and found that the hexane fraction was the most effective fraction in activating Nrf2-mediated suppression of iNOS expression in macrophages. Utilizing preparative, reverse-phase HPLC and a comparative analysis by analytical scale LC-UV, we found the hexane fraction contains predominantly polyacetylenes and linolenic acid. Moreover, we identified panaxynol, one of the major polyacetylenes, to be a potent Nrf2 activator, and to suppress the inflammatory responses in macrophages as well as the pro-atherogenic interaction between vascular smooth muscle cells and macrophages. These results provide a potential mechanism responsible for the American ginseng-mediated health benefits. Because panaxynol also exists in a variety of other foods, a comprehensive understanding of the dietary component-mediated Nrf2 signaling in the vasculature will provide novel insight into the adoption of desirable dietary behaviors as well as the development of unique therapeutic approaches against vascular diseases.

CV09 The effect of low plasma estrogen on mesenteric arterial function in female mice

J. Daniel Fleming
Graduate Student, University of Central Arkansas
bhill@uca.edu

J. Daniel Fleming, Charmain A. Fernando1, William R. Gray1, Shi J Liu2, and Brent J.F. Hill1 1Department of Biology, University of Central Arkansas, Conway, AR 2Department of Pharmaceutical Sciences, University of Arkansas for Medical Sciences, University of Arkansas for Medical Sciences, Little Rock, AR

Circulating plasma estrogen (E2) protects women against the development of abnormal vascular tone which is often associated with the enhanced Ca2+ entry into smooth muscle cells (SMCs) via voltage-gated Ca2+ channels (VGCCs). The purpose of this study is to determine the effect of E2 deficiency on VGCCs. Female mice (C57BL/6) were instrumented for biotelemetry at 7 wks of age. At 8 wks, the mice underwent an ovariectomy (OVX) or sham surgery. Biotelemetry measured a drop in heart rate 2 wks post-OVX surgery suggesting a baroreceptor reflex compensation. At 12 wks the mice were sacrificed. The OVX mice had a decline in their plasma E2 concentration. They also exhibited atrophied uterus and weight gain. The mesenteric arteries were isolated and pressurized at 80 mmHg to measure arterial reactivity to the VGCC agonist, FPL64176 (3x10-7 to 1x10-6 M); there was no difference between groups in their spontaneous tone and response to FPL64176. Western blots showed a slight increase (p=0.12) in the pore-forming alpha1C subunit of the VGCC. There was no change in the VGCC beta1 subunit. Smooth muscle cells (SMCs) were isolated from the arteries to conduct fluorescent imaging of the SMCs loaded with the ratiometric calcium indicator, fura-2AM. There was an enhanced fura-2 ratio in cells from OVX mice exposed to the VGCC agonist, FPL64176 (p=0.03). However, when the sarcoplasmic reticulum (SR) was Ca2+ depleted (using the ryanodine receptor agonist, caffeine, and the SR Ca2+-ATPase pump inhibitor, thapsigargin) before exposing the cells to FPL64176 there was no difference in the fura-2 ratio between OVX and sham mice. This suggests that the SR contributes to the enhanced VGCC-mediated entry of Ca2+ into SMCs. Overall, our results indicate that the decline in E2 in women can enhance Ca2+ entry into SMCs. Long-term this may lead to an elevation in arterial tone and blood pressure in resistance arteries. Support: NIGMM of the NIH, Grant #P20 GM103429-11.
CV10  Effects of Blocking Cell-Cell and Cell-Matrix Interactions on Mechanical Properties of Cardiomyocytes

Aesha Desai & Evan Robinson
Undergraduate Student, Clemson University
ejrobin@clemson.edu

Aesha Desai & Evan Robinson, Sandra Deitch, Delphine Dean

Introduction: Cardiovascular diseases like atherosclerosis are the number one cause of death in United States. In an atherosclerotic artery, vascular smooth muscle cells (VSMCs) undergo a phenotypic shift; enter the intima layer and deposit extracellular matrix which makes the cellular environment very heterogeneous. Based on our hypothesis, we studied the effects of blocking cell-cell (N-cadherin) and cell-matrix (integrin B1) on VSMCs. The results showed that VSMCs under such conditions were less stiff, more relaxed, and took on a more synthetic phenotype after 5 days in culture. Our current study focuses on blocking cell-cell and cell-matrix interactions in cardiac cells (cardiomyocytes). Methods and Materials: Neonatal cardiomyocytes dissected from day 3 rat hearts are used and seeded at a density of 20,000 cells/cm² and cultured for 5 days. Different media conditions used: regular media (DMEM+10%FBS +1%anti/anti), regular media with 50μg/ml integrin β1 antibody, regular media with 50μg/ml of N-cadherin antibody, regular media with both the antibodies, control with IgG. Atomic Force Microscopy and Cytoindentation experiments are performed at day 5. Immunofluorescence imaging is used to confirm antibody blocking. Results and Discussion: Blocking N-cadherin and integrin β1 interactions individually and in combination on VSMC’s resulted in greatly reduced cellular elastic moduli and increased cellular percent relaxation measures. Analysis of cardiomyocyte data is ongoing. Conclusion: From VSMC studies we concluded that the cells under test conditions were more homogeneous in their mechanical properties than cells under control conditions. We hope to observe similar results in cardiac cell studies to better understand cellular mechanical heterogeneity and incorporate them in tissue level models. Currently, we are studying the co-culture of cardiomyocytes and cardiac fibroblasts and plan on doing blocking studies in co-culture as well.

CV11  Estrogen-mediated mechanisms for the regulation of voltage-gated, calcium channels in coronary arteries

Mohamed Idrissa Moussa
Undergraduate Student, University of Central Arkansas
bhill@uca.edu

Mohamed Idrissa Moussa, Edouard Niyonsaba1, Robin J. Dalton1, Nancy J. Rusch2, Brent J.F. Hill1 1Department of Biology, University of Central Arkansas, 201 Donaghey Ave., Conway, AR  2Pharmacology & Toxicology, University of Arkansas for Medical Sciences, Little Rock, AR

Many vascular dysfunctions demonstrate an upregulation of voltage-gated, L-type Ca2+ channels (VGCCs). Previously, our lab has shown that estrogen (E2) can downregulate VGCCs. The aim of this study is to determine the mechanisms associated with this E2-induced downregulation. The right coronary artery was obtained from hearts of female pigs. The coronary arteries were sectioned into longitudinal strips (Western blots, real-time PCR) or rings (isometric tension) and incubated for 24 hrs in 1nM E2 or EtOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually incubated for 24 hrs in 1nM E2, ETOH (E2 solvent). Total mRNA was isolated and the relative mRNA abundance was determined using real-time PCR. There was similar abundance of the alpha1C transcript between EtOH and E2 treated arteries. This suggests that the E2-induced downregulation of VGCCs are posttranscriptionally regulated. To determine if the downregulation occurred via estrogen receptors (ER) the arterial strips were individually inc...
CS06 A Comparative Genomics Approach to Link Plant and Animal Oxidative Stress Signaling Pathways

John Butler and Kirby Von Edwins
Undergraduate Student, Ouachita Baptist University, Arkansas
but49035@obu.edu

John Butler and Kirby Von Edwins, Nathan Reyna (Ouachita Baptist University)

Oxidative stress is known to damage living organisms. Any organism that is better equipped to deal or alleviate oxidative stress is more likely to survive and reproduce. Being able to induce small amounts of oxidative stress is thought to prepare plants for future doses of large oxidative stress; turning on certain defense signaling pathways before the large stress presents itself allows for plants to alleviate stress more efficiently. Using tobacco plants that have been transfected with the glucose oxidase (GOx) gene, we are able to introduce small amounts of stress to the plants in the form of over production of hydrogen peroxide, a reactive oxygen species (ROS). With extra ROS present in the transfected tobacco plants, a “vaccine-effect” is expected to be seen when faced with oxidative stresses and other types of stress, such as drought-stress, as opposed to the wild-type which would be more harshly affected by all stress. To demonstrate this, an experiment was set up with our transfected plants to be put in a drought test and durability throughout the drought would be measured versus the wild-type. The expected result is that our transfected tobacco plants are better equipped to handle all types of stress due to the stress-relieving pathways already being turned on by the GOx gene.

CS07 Mitochondrial fission and fusion in Dictyostelium discoideum: a search for proteins involved in membrane dynamics

Kari Naylor, Ph.D.
Assistant Professor, University of Central Arkansas
kknaylor@uca.edu

Kari Naylor, Brixey Schimmel- UCA Greg Berbusse-UCA Laken Woods- UCA

Mitochondrial morphology is maintained by two distinct membrane events -fission and fusion. Altering these conserved processes can disrupt mitochondrial morphology and distribution, thereby disrupting the organelle’s functionality and impeding cellular function. In higher eukaryotes, these processes are mediated by a family of dynamin-related proteins (DRP’s). While in lower eukaryotes, such as Dictyostelium discoideum, mitochondrial fission and fusion have been implicated but not yet established. To understand the overall mechanism of these dynamics across organisms, we developed an assay to identify fission and fusion events in Dictyostelium and to assess the involvement of the mitochondrial proteins, MidA, CluA, and two DRPs, DymA and DymB. Here we show that in Dictyostelium, fission and fusion events are balanced, occurring approximately 1 event/minute. Quantification of the rates of fission and fusion in midA-, cluA-, dymA-, or dymB- strains established that MidA appears to play an indirect role, while the DRP’s are not essential for these processes. Rates of fission and fusion were significantly reduced in cluA- cells, suggesting that CluA is necessary for maintaining both fission and fusion. Mitochondrial dynamics are intimately linked to mitochondrial motility thus we have also assessed the motility of the mitochondria in these mutants to ensure there is no underlying motility defect. Our preliminary data suggests that there is no change in the rate of mitochondrial movement in any of these strains. In conclusion, we have determined that remarkably DRP’s are not essential for fission and fusion in D. discoideum and CluA – a protein found in yeast, plants, and flies with no known function- plays a role in both processes.
CS08 Mapping the binding site of the C-terminal domain of Alb3 on the Chromodomains of cpSRP43

Srinivas Jayanthi, Ph.D.
Post Doctoral Research Associate, University of Arkansas
sjayanth@uark.edu

Srinivas Jayanthi, Srinivas Jayanthi1, Jake Usery1, Rory Henderson1, Mercede Furr1, Alicia Kight2, Robyn Goforth2, Ralph Henry2, T.K. S. Kumar2 1. Department of Chemistry and Biochemistry; 2. Department of Biological Sciences University of Arkansas, Fayetteville, AR 72701

Chloroplast Signal Recognition Particle (cpSRP), comprising of cpSRP43 and cpSRP54 subunits, plays an important role in the post-translational integration of the Light Harvesting Chlorophyll Binding Protein (LHCP), into the thylakoid membrane. Recently, it has been demonstrated that C-terminus portion of Alb3 (C-term Alb3), an integral membrane protein, interacts with the 43kDa subunit of cpSRP (cpSRP43). The present study is focused on understanding the structural interactions between cpSRP43 and C-term Alb3. Peptides spanning the amino acid sequence of C-term Alb3 were synthesized and their individual binding affinity to the C-terminal chromodomain (CD2-CD3) of cpSRP43 was examined using isothermal titration calorimetry. One of the C-term Alb3 peptides, Motif4 (mC-term Alb3), showed strong binding affinity to both the CD2-CD3 domain (Kd ~ 8 micromolar) and the full length cpSRP43 (Kd~ 14 micromolar). The three-dimensional solution structure of the CD2-CD3 domain was determined at high resolution to elucidate the binding interface between mC-term Alb3 and the CD2-CD3 domain. Results of the 1H-15N chemical shift perturbation experiments revealed that acidic residues, Glu327 and Glu356, in the CD2-CD3 domain are critical for the C-term Alb3/CD2-CD3 interaction. ITC data show that site-specific mutants, Glu327Lys & Glu356Lys, of CD2-CD3 exhibit no significant binding affinity to mC-term Alb3. Interestingly, results of the in vitro integration assays suggest that the loss of interactions between mC-term Alb3 and the CD2-CD3 domain of cpSRP43 do not significantly affect the integration of LHCP into the thylakoid membrane. The significance of these results in the post-translational targeting of LHCP to the thylakoid will be presented in detail.

CS09 Structural Flexibility and Allostery in cpSRP43 Revealed by Single Molecule FRET

Feng Gao, Ph.D.
Post Doctoral Research Associate, University of Arkansas
fg003@uark.edu

Feng Gao1, Alicia D. Kight2, Parth Patel1, Priyanka Sharma2, Robyn L. Goforth2, Ralph L. Henry2, and Colin D. Heyes1,* 1Department of Chemistry and Biochemistry, University of Arkansas, Fayetteville, AR 72701 2Department of Biological Sciences, University of Arkansas, Fayetteville, AR 72701

The chloroplast signal recognition particle (cpSRP) consists of a heterodimer of proteins, cpSRP43 and cpSRP54, and is responsible for transporting the hydrophobic light harvesting chlorophyll-binding protein (LHCP) into the thylakoid membrane for photosynthesis. To better understand the structure-dynamics-function relationship of the cpSRP, we present a single molecule Förster Resonance Energy Transfer (smFRET) study on the interdomain structural dynamics of cpSRP43, a unique multidomain protein consisting of 3 chromodomains (CD) and 4 Ankyrin domains (Ank). Our smFRET results reveal that the structure of cpSRP43 is very flexible, adopting a wide range of dynamically interconvertible conformations, and undergoes long-range (allosteric) conformational changes upon binding cpSRP54. The smFRET results allows us to dissect several structural features contributing to the observed structural flexibility and allostery, including specific interactions between the CD1-Ank4 and the CD2-CD3 regions of cpSRP43, a swinging motion of the ~2.5 nm long α helix in Ank4 and allosteric conformational changes in another ~2.5 nm long α helix connecting the CD1 and Ank1 domains. Besides regulating allosteric conformational changes in cpSRP43, a major effect of cpSRP54 binding to cpSRP43 is to reduce the structural flexibility of cpSRP43. We use these results to propose an “interaction funnel” analogous to the “folding funnel” that relates the reduction in the protein flexibility to the various interdomain interactions, which may be used to rationalize the ability of cpSRP43 to sequentially bind multiple substrates, which underlies its function of transporting and incorporating LHCP into the thylakoid membrane.
CS10 Restoration of somatotrope function in vitro by ghrelin in male mice lacking the signaling domain of leptin receptor

Mohsin Syed, Ph.D.
Assistant Professor, University of Arkansas for Medical Sciences
syedmohsinm@uams.edu

Cozart, M, Akhter, N, Haney, AC, Odle, A, Allensworth-James, M, Syed, FM and Childs, GV Neurobiology and Developmental Sciences, University of Arkansas for Medical Sciences

Selective ablation of the leptin receptors exon 17 in somatotropes, with Cre-loxP technology, resulted in growth hormone deficiency and a reduction in the percentage of immunolabeled GH cells. We hypothesized that the deficit is caused by the failure of leptin’s postnatal surge to stimulate an expansion in the cell population. To learn more about the deficiency in GH cells, we tested their expression of GHRH receptors and GH mRNA and the restoration by secretagogue (ghrelin) stimulation in vitro. In freshly dissociated pituitary cells from control male mice, GHRH alone (0.3 nM) increased the percentage of immunolabeled GH cells from 27 ± 0.05% (vehicle) to 42 ± 1.8% (P < .002) and the secretion of GH 1.8-3×. Deletion mutant pituitary cells showed a 40% reduction in percentages of immunolabeled GH cells (16.7 ± 0.4%), which correlated with a 47% reduction in basal GH levels (50 ng/mL control; 26.7 ng/mL mutants P = .01). A 50% reduction in the percentage of mutant cells expressing GHRH receptors (to 12%) correlated with no or reduced responses to GHRH. Ghrelin alone (10 nM) stimulated more GH cells in mutants (from 16.7-23%). When added with 1-3 nM GHRH, ghrelin restored GH cell percentages and GH secretion to levels similar to those of stimulated controls. The number of somatotropes labeled for GH mRNA confirmed that there were normal percentages of somatotropes in the population. The real-time qRT-PCR experiments also confirmed normal levels of GH-mRNA in the deletion mutant animals. These discoveries indicated that somatotropes are present but quiescent in the absence of leptin receptor, suggesting leptin’s importance in optimizing somatotrope function by posttranscriptional mechanisms.

Perhaps leptin facilitates translation of GHRHR or GH mRNAs, regulating protein stores in preparation for secretion. Supported by: NIH1R01HD059056(GVC); NIHNCRRP20RR020146; NIHP30NS047546, NIHR03HD059066(GVC).

CS11 Selective Ablation of Leptin Receptor JAK Binding Site in Somatotropes Alters Metabolic Status Causing Adult Onset Obesity

Noor Akhter, Ph.D.
Assistant Professor, Department of Neurobiology and Developmental Sciences, College of Medicine, University of Arkansas for Medical Sciences, Little Rock, AR
AkhterNoor@uams.edu

Noor Akhter, Ph.D., Antela Odle, Melody Allensworth, Anessa Haney, Mohsin Syed, and Gwen V. Childs

Mice with somatotrope-specific deletion of the Janus Kinase (JAK) binding site in leptin receptors are GH deficient and obese by 6 months of age. This study focused on the metabolic status of young (3-4.5 month old) preobese mutant mice, which had normal body weights, lean body mass, serum leptin, glucose, and triglycerides. Mutants showed significantly higher respiratory quotients (RQ) and lower energy output, resulting from a higher volume of CO2 output and lower volume of O2 consumption. Deletion mutant females were significantly less active than controls; with higher serum ghrelin and food intake. Mutant females also had lower serum insulin and higher glucagon. In contrast, deletion mutant males were not hyperphagic, but they were more active and spent less time sleeping. Adiponectin and resistin, products of adipocytes, were increased in both male and female mutants. In addition, mutant males showed an increase in circulating levels of the potent lipogenic hormone, glucose-dependent insulino inhibotic peptide. Taken together, these results indicate that mutant mice may become obese due to a reduction in lipid oxidation and energy expenditure, stemming from GHD. Reduced fat oxidation and enhanced insulin sensitivity (in females) are directly related to GHD in mutant mice because GH has been shown by others to increase insulin sensitivity and fat oxidation and reduce carbohydrate oxidation. Gender-dependent alterations in metabolic signals may further exacerbate the future obese phenotype and affect the timing of its onset. Females show a delay in onset of obesity, perhaps because of their low serum insulin, which is lipogenic, whereas young males already have higher levels of the lipogenic hormone, glucose-dependent insulino inhibotic peptide. These findings signify that leptin signals to somatotropes are vital for the normal metabolic activity needed to optimize body composition. Support: NIH1R01HD059056 (GVC); NIH NCRR P20 RR020146; NIHP30 NS047546, R03 HD059066 (GVC).
CS12  Selective Ablation of Leptin Receptor Signaling in Gonadotropes Reduces Serum Gonadotropins and Fertility in Female Mice

Gwen V. Childs, Ph.D.
Professor, University of Arkansas for Medical Sciences
childsgwen@uams.edu

Gwen V. Childs, Ph.D., Mohsin Syed, Tyler CarlLee, Michael Cozart, Noor Akhter, Anessa Haney, Angela Odle and Melody Allensworth; Department of Neurobiology and Developmental Sciences, College of Medicine, University of Arkansas for Medical Sciences, Little Rock, AR 72205

Leptin regulates appetite and metabolism, permitting the onset of puberty and reproduction. To determine leptin’s regulatory role for gonadotropes, we crossed mice bearing LEPRexon17 loxP/loxP with mice bearing Cre-recombinase (Cre) driven by the LHβ promoter (Cre-LHβ), thereby ablating LEPR signaling selectively in gonadotropes. Organ genotyping proved selective pituitary Cre expression only in females. Serum LH and GH were lower in 19 deletion mutant males (ng/ml--0.9±0.2 LH; 3.5±1 GH) compared with 26 littermate controls (ng/ml--2.2±0.5 LH; 11.2±2.8 GH) p<0.01. In vitro studies showed that, after 1 h exposure to 0-30 nM GnRH, cultures from mutants secreted 63% less LH and 55% less FSH basally than controls and showed a blunted response to 0.1-1 nM GnRH with 30-64% less LH and 27% less FSH. Breeding studies detected normal timing of puberty, first litter, or time between litters in male or female mutant parents. Litters (n=9) from mutant (Cre-LHβ+) males and Cre-neg. females averaged 8.8±0.7 pups/ litter, which was not different from the average seen in 6 litters from the same-strain control animals (FVB.129S--9.3±0.7 pups/litter). In contrast, 9 litters from mutant Cre-LHβ+ females and Cre-negative males averaged only 5.5 ±1.4 pups/litters, which was significantly lower than those from the mutant males or the control strain (p<0.03). These studies suggest that leptin’s signaling to pituitary gonadotropes helps maintain serum levels of LH and GH, in vivo. Mutant females clearly show a 40% reduction in number of pups/litter. The impact of lack of leptin signaling is also seen dramatically in vitro by the blunted responses to physiological doses of GnRH. Perhaps, when the timing and metabolic conditions are appropriate, leptin signaling optimizes gonadotropin stores to facilitate rapid responses to pulses of GnRH and insure reproductive success. Supported by NIH 1R01HD059056 (GVC); NIH NCRR P20 RR020146; NIH P30 NS047546 (core), NIH R03 HD059066 (GVC).

CS13  Investigation of the role [4Fe-4S] clusters play in RNA polymerase assembly and function

Matthew Jennings
Graduate Student, University of Arkansas
mej013@uark.edu

Matthew Jennings, Faith H. Lessner -1 Elizabeth A. Karr - 2 Daniel J. Lessner - 1 1- Department of Biological Sciences, University of Arkansas, Fayetteville, AR 72701 2- Department of Botany and Microbiology, University of Oklahoma, Norman, OK 73019

Several species of the Archaea and the Eukarya contain a [4Fe-4S] cluster binding motif(s) within domain 3 of the D/Rpb3 subunit of RNA polymerase (RNAP); the function of the [4Fe-4S] cluster(s) is unknown. We have recently used a recombinant approach to demonstrate that subunit D of RNAP from the anaerobic archaeon Methanosarcina acetivorans contains two oxygen-labile [4Fe-4S] clusters, which impact the stability of the D/L heterodimer, the first step in the assembly of RNAP. We hypothesize the [4Fe-4S] clusters provide a mechanism to correlate transcription with metabolism by regulating RNAP assembly and/or activity in response to the redox state of the cell. To ascertain the importance of the [4Fe-4S] clusters in vivo we have developed two approaches using the genetic system in M. acetivorans. Each approach employs a set of subunit D variants where the [4Fe-4S] cluster binding motifs have been mutated or deleted. The first approach utilizes inducible expression of affinity-tagged D variants to examine RNAP assembly using pull-down assays. Initial results reveal that domain 3 is not essential for interaction of subunit D with subunit L; however changes to domain 3 do impact assembly of other RNAP subunits. The second approach involves replacement of native subunit D in M. acetivorans with variant D subunits. Viable strains have been generated expressing subunit D without domain 3, and subunit D where the [4Fe-4S] cluster motif #2 has been mutated, however both strains have an impaired growth phenotype. Viable strains expressing domain 3 with individual cluster deletions have not been generated. Our data indicates the [4Fe-4S] clusters within domain 3 of subunit D may serve to regulate RNAP assembly and/or activity in vivo.
CS14  Defining Mechanisms of Reovirus Cell Killing

Johnasha Stuart
Graduate Student, University of Arkansas for Medical Sciences
jstuart2@uams.edu

Johnasha Stuart1, 2, Bernardo A. Mainou3, 4, Terence S. Dermody3, 4, and Karl W. Boehme1, 2  1Department of Microbiology and Immunology, 2Center for Microbial Pathogenesis and Host Inflammatory Response, University of Arkansas for Medical Science, Little Rock, AR, 3Department of Pediatrics and 4Elizabeth B. Lamb Center for Pediatric Research, Vanderbilt School of Medicine, Nashville, TN.

Host cell death is fundamental to the process for viral pathogenesis. Recent advances have identified new cell killing mechanisms and redefined the biochemical hallmarks that characterize cell death pathways. However, it is not known how these pathways function in the context of viral infection or contribute to viral disease. Mammalian orthoreovirus (reovirus) is a highly tractable model for studying virus-induced cell death in cultured cells and in vivo. Reoviruses use serotype-specific mechanisms to kill cells. Serotype 3 (T3) reoviruses induce apoptosis, whereas serotype 1 (T1) reoviruses kill cells through a non-apoptotic pathway. A genome-wide siRNA screen to define host genes required for reovirus-induced cell death identified receptor interacting protein 1 (RIP1) as a mediator of reovirus cell killing. RIP1 occupies a central node in cell death signaling that translates death stimuli into apoptotic or non-apoptotic cell killing pathways. We found that Necrostatin-1 (Nec-1), an inhibitor of RIP1 kinase activity, prevented T1, but not T3 reovirus-induced cell killing. This finding indicates that T1 reovirus causes non-apoptotic cell death via programmed necrosis. Nec-1 did not reduce viral progeny production from infected cells, indicating that Nec-1 does not impair cell death by inhibiting viral replication. This research will characterize the mechanistic basis of reovirus-induced cell death and facilitate studies to determine how different modes of cell killing contribute to viral pathogenesis.

CS15  Mitochondrial fission and fusion in Dictyostelium discoideum: a search for proteins involved in membrane dynamics

Greg Berbusse
Graduate Student, University of Central Arkansas
kknaylor@uca.edu

Greg Berbusse, Brixey Schimmel-UCA Laken Woods-UCA Kari Naylor-UCA

Mitochondrial morphology is maintained by two distinct membrane events - fission and fusion. Altering these conserved processes can disrupt mitochondrial morphology and distribution, thereby disrupting the organelle’s functionality and impeding cellular function. In higher eukaryotes, these processes are mediated by a family of dynamin-related proteins (DRP’s). While in lower eukaryotes, such as Dictyostelium discoideum, mitochondrial fission and fusion have been implicated but not yet established. To understand the overall mechanism of these dynamics across organisms, we developed an assay to identify fission and fusion events in Dictyostelium and to assess the involvement of the mitochondrial proteins, MidA, CluA, and two DRPs, DymA and DymB. Here we show that in Dictyostelium, fission and fusion events are balanced, occurring approximately 1 event/minute. Quantification of the rates of fission and fusion in midA-, cluA-, dymA-, or dymB- strains established that MidA appears to play an indirect role, while the DRP’s are not essential for these processes. Rates of fission and fusion were significantly reduced in cluA- cells, suggesting that CluA is necessary for maintaining both fission and fusion. Mitochondrial dynamics are intimately linked to mitochondrial motility thus we have also assessed the motility of the mitochondria in these mutants to ensure there is no underlying motility defect. Our preliminary data suggests that there is no change in the rate of mitochondrial movement in any of these strains. In conclusion, we have determined that remarkably DRP’s are not essential for fission and fusion in D. discoideum and CluA – a protein found in yeast, plants, and flies with no known function- plays a role in both processes.
CS16  RNA-seq analysis reveals the differential expression of Hoxa1 target genes in mouse ES cells in response to retinoic acid

Danielle M. Refuge  
Graduate Student, Southern University and A & M College  
danielle_refuge_00@subr.edu

Danielle M. Refuge, Xiaoping Yi and Eduardo Martinez-Ceballos Southern University and A&M College

The homeobox (Hox) family of transcription factors comprises important regulators of embryonic patterning and organogenesis. In mammals, the Hox genes are located in four separate chromosome clusters, Hoxa, Hoxb, Hoxc and Hoxd and their expression depends on their position in the chromosomal cluster: genes positioned at the 3’ end are expressed earlier and more anteriorly than 5’ end genes. In addition, Hox genes can be activated sequentially by retinoic acid (RA) in a manner that resembles their positions in the clusters, e.g. 3’ genes are activated by RA before 5’ genes. In vertebrate embryos, alterations of the normal pattern of Hox gene expression result in homeotic transformations and malformations. In mice, disruption of the Hoxa1 gene results in abnormal ossification of the skull, hindbrain, inner ear deficiencies, and neonatal death; however, little is known about the molecular events that occur downstream of Hoxa1 gene activation. In an attempt to elucidate the molecular mechanism of Hoxa1 action in mouse Embryonic Stem (ES) cells, gene expression profiling was carried out on Wild type versus Hoxa1-/- mouse ES cells using RNA-seq. Overall, transcriptome profiling revealed significant changes in the expression of 2842 genes. Of these, 1979 genes were upregulated by RA in Wt ES cells and 863 were downregulated in these cells as compared to Hoxa1-/- ES cells. The gene ontology of the differentially expressed genes is discussed further. These results provide an insight into the mechanism of Hoxa1 action in differentiating mouse ES cells.

CS17  Musashi interacts with a large “effectome” to mediate sequence-specific mRNA translational control

Chad Cragle  
Graduate Student, University of Arkansas for Medical Sciences  
Angus@UAMS.edu

Chad Cragle, MacNicol, M.C., Center for Translational Neuroscience, University of Arkansas for Medical Sciences Hardy, L.L., Center for Translational Neuroscience, University of Arkansas for Medical Sciences Tackett, A., UAMS MacNicol, A.M., University of Arkansas for Medical Sciences

During early vertebrate development, regulated mRNA translation is essential to control gene expression in a highly orchestrated spatiotemporal manner for cell cycle progression. Our recent work has revealed a hierarchical, sequential program of mRNA translational control involving Pumilio, Musashi and CPEB. While considerable progress has been made in understanding Pumilio- and CPEB-mediated control, much less is known concerning the effectors of Musashi-dependent mRNA translational regulation and how Musashi action is functionally integrated with downstream CPEB activity. We report identification and characterization of Musashi effectors proteins, including the non-canonical poly[A] polymerase GLD2 and the embryonic poly[A] binding protein, ePAB. GLD2 and ePAB map to a shared 40 amino acid domain on Musashi1. Overexpression of GLD2 synergizes with Musashi to promote target mRNA translation and accelerate cell cycle progression. Inhibition of endogenous ePAB synthesis specifically attenuates Musashi-dependent mRNA translation, feedback amplification of Musashi activation and blocks cell cycle progression. These results couple Musashi1 to both polyadenylation and translational initiation complexes. Interestingly, the Musashi2 isoform displays dramatically reduced affinity for ePAB and notably, has reduced biological activity to promote cell cycle progression. These results are consistent with a positive role for ePAB interaction driving translation of Musashi target mRNAs. Our mass spectrometry analyses have also identified a number of unexpected Musashi-associated proteins including several distinct sequence-specific RNA binding proteins. The significance of these interactions for the integration and timing of mRNA translation during cell cycle control will be discussed.
In general, transmembrane alpha-helices are composed of primarily hydrophobic residues and contain very few strongly polar amino acids. Although sparse, hydrophilic residues tend to be highly conserved if present in transmembrane domains, indicative of their importance in the structure or function of the protein. Synthetic model peptides such as GWALP23 (acetyl-GGALWSLALALALALALALW19LAGA-amide) are useful probes to investigate the influence of polar amino acids within the hydrophobic core of a transmembrane helix. To investigate histidine residues in lipid bilayer membranes, we have employed GWALP23 as a favorable host peptide. Importantly, membrane-spanning GWALP23 is quite sensitive to single-residue replacements, in part because the transmembrane helix exhibits only limited dynamic averaging of solid-state NMR observables such as the 2H quadrupolar splitting (Biophys. J. 101, 2939). We inserted His residues into position 12 and/or 13 of GWALP23 (replacing either L12 or A13) and incorporated specific 2H-Ala labels within the helical core sequence. Solid-state 2H NMR spectra reveal a marked difference between the L12H mutant and the L12H-A13H double mutant. At neutral pH, GWALP23-H12 exhibits a well-defined tilted transmembrane orientation in both DOPC and DLPC bilayer membranes. Under acidic conditions, however, GWALP23-H12 is highly dynamic and exhibits multiple states which are in slow exchange on the NMR timescale. Indeed, the multi-state behavior of GWALP23-H12 between pH 1.5 and pH 3 resembles closely that of GWALP23-R12 at neutral pH (J. Am. Chem. Soc. 132, 5803). By contrast, GWALP23-H12,13 aggregates over a pH range of 4-9, which remains puzzling. Further aspects of the pH dependence of transmembrane helices having one or two histidines are under investigation.

Induction of PKC isoforms during Coxiella burnetii infection of THP-1 macrophages

Lucas DeYoung
Undergraduate Student, John Brown University
jofunk@jbu.edu

Lucas DeYoung, Chad Schlagel and C. Joel Funk.

Q fever is a zoonotic disease that begins as a respiratory illness and causes flu-like symptoms. The disease is initiated as Coxiella burnetii enters alveolar macrophages and manipulates the host cell into forming a bacterial replication vacuole, called a parasitophorous vacuole (PV). As an intracellular bacterial pathogen, C. burnetii interacts with the host cell and redirects the normal endosome-lysosome pathway in favor of PV formation. Previous studies using inhibitors have indicated C. burnetii uses host kinase activity as part of this manipulation of the host. More specifically, protein kinase C (PKC) has been demonstrated to be involved in PV formation. However, since ten PKC isoforms have been described, the focus of this study was to decipher which isoform(s) are involved in C. burnetii infection. We examined the role of PKC isoforms -alpha, -beta, -delta, -epsilon, -eta, and -zeta using immunoblot analysis. THP-1 monocyte cells were differentiated into macrophages, infected with an avirulent C. burnetii strain and harvested over a 96 hour time period. The activity of each isoform was assessed by probing with antibodies made against both total and phospho-specific versions of each PKC isoform. Although the total amount of each PKC isoform can vary at each time point, the blots indicated increased levels of activated PKC-alpha, -betaII, and –eta during the C. burnetii infection and a decrease in –delta activation during late stages of the infection. The ability to understand crucial kinase signaling events during infection by C. burnetii will be useful for the evaluation of drug targets and for the development of small molecule inhibitors.
**CS20**  
Mitochondrial fission and fusion require an intact cytoskeleton

Jordyn Cleavenger  
Undergraduate Student, University of Central Arkansas  
kknaylor@uca.edu

The cytoskeleton functions in a myriad of cellular processes. One of these processes is organelle movement. To understand the role of the cytoskeleton in mitochondrial motility, fission, and fusion, we are analyzing these processes in a Dictyostelium discoideum cluA- strain. D. discoideum cells lacking CluA have clustered mitochondria that are connected via narrow tubules; these mitochondria have decreased rates of fission and fusion. It has been argued that CluA may link the mitochondria to the cytoskeleton, though in the absence of CluA the rate of motility is unchanged. Using the chemotherapeutics nocodazole and latrunculin B, we are determining the rates of mitochondrial fission, fusion, and motility when the cytoskeleton is disrupted. Our preliminary results indicate that microtubules are necessary for both fission and fusion in wild-type and cluA- strains. Microtubules are necessary for mitochondrial motility in mammalian cells thus these results suggest that mitochondrial motility is required for fission and fusion to take place. This work also gives us some insight into the role of CluA, as fission and fusion rates in cluA- cells decreases even more with disrupted microtubules; we would argue that CluA is not involved in linking the mitochondria to the cytoskeleton. In conclusion we have shown that microtubules play a significant role in the mitochondrial fission and fusion processes of D. discoideum cells. As we continue to study the cytoskeleton’s role in fission and fusion we will gain insight into mitochondrial diseases resulting from defects in these processes.

---

**CS21**  
N-acetylcysteine inhibits liver mitochondrial biogenesis in rats fed alcohol chronically

Shannon Ejiofor  
Undergraduate Student, Chemistry Department, Hendrix College  
caro@hendrix.edu

Chronic alcohol administration to rats induces liver oxidative stress and mitochondrial biogenesis. The mechanisms by which chronic alcohol induces mitochondrial biogenesis have not been fully explored. In this work, we hypothesized that oxidative stress is a factor that triggers mitochondrial biogenesis in chronically alcohol-fed rats. If our hypothesis is correct, then the co-administration of antioxidants should prevent alcohol-induced mitochondrial biogenesis. Rats were administered alcohol intragastrically for 150 days, in the absence or presence of the antioxidant N-acetylcysteine (NAC) at 1.2 g/kg/day; control rats were administered an isocaloric diet. Liver redox state was evaluated by the levels of GSH and GSSG, which were determined by an enzymatic recycling method. Alcohol administration significantly decreased the GSH/GSSG ratio with respect to the controls and NAC prevented this decrease. This result shows that alcohol caused liver oxidative stress and that NAC was an antioxidant in our model. Mitochondrial biogenesis was evaluated biochemically using the following markers: mRNA and protein levels of peroxisome proliferator activated receptor gamma-coactivator 1 alpha and mitochondrial transcription factor A, and mitochondrial DNA levels. Mitochondrial biogenesis markers were increased by alcohol and this increase was prevented by NAC. In addition, chronic alcohol administration was associated with inactivation and depletion of mitochondrial complex I and complex IV (but not complex II), effects that were partially prevented by NAC. Mitochondrial DNA (but not nuclear DNA) integrity decreased significantly in alcohol-treated livers, an effect partially prevented by NAC. These results suggest that oxidative stress caused by chronic alcohol triggers liver mitochondrial dysfunction and biogenesis.
GM03 A Radial Diffusion Assay for the Rapid Evaluation of Antimicrobial Peptides

Dustin Walter
Undergraduate Student, Ouachita Baptist University, Arkansas
wal51422@obu.edu

Dustin Walter*, Yazan Akkam2,3, and David S. McNabb2,3

Ouachita Baptist University, Arkadelphia, AR1, Department of Biological Sciences and the Cell and Molecular Biology Program, University of Arkansas, Fayetteville, AR2,3

Antimicrobial peptides (AMPs) have been a major research focus due to their potential to combat a variety of human pathogens. Our laboratory has identified several novel peptides that display significant antifungal activity. The effectiveness of these peptides in vitro has proven promising; however, it has been shown that physiological concentrations of various salts along with other conditions are inhibitory to the activity. To further explore the inhibitory effects of these salts, a new assay was developed whereby we can observe the effects of various salts on the peptide killing activity. For our studies, we employed several clinical isolates of Candida species to evaluate the killing activity of peptides in the presence of physiologically relevant salts at varying concentrations. By adding the salts individually, we are able to examine the inhibitory effect of each. When compared to other assays, the new assay requires less time and resources by allowing us to test the AMPs under numerous conditions simultaneously. After testing the AMPs, we determined that CaCl2, MgSO4, NaCl, and KCl are all inhibitory to peptide killing activity at varying degrees. In addition, we discovered that circularization or hexanoic acid modification of the peptide bypasses the inhibition of salts. Our long term goal is to modify the peptides in a way that will allow for their use in vivo.

GM06 Analysis of polymeric gels for the transdermal delivery of capsaicin for the treatment of chronic low back pain

Jennifer Greene
Undergraduate Student, School of Pharmacy, University of Charleston, WV
jennifergreene@go.ucwv.edu

Jennifer Greene, A. Almeida†, U.K. Reddy‡, and G. Kaushal†* †School of Pharmacy, University of Charleston, Charleston, WV
*Jefferson School of Pharmacy, Thomas Jefferson University, Philadelphia, PA ‡Gus R. Douglass Institute and Department of Biology, West Virginia State University, Institute, WV

Purpose Our objective is to develop value added pepper varieties adapted to local conditions and extract this natural capsaicin from these peppers to formulate a transdermal gel for chronic back pain. Methods An HPLC method was developed that could quantify between the two major components of capsaicinoids: capsaicin and dihydrocapsaicin. Eighty-eight Capsicum annuum cultivars were grown and fruits were collected 30 days after pollination. Peppers were chopped and oven dried at 55°C and grounded to a powder. Capsaicin was extracted according to the standard procedure and the samples were further process by solid phase extraction (SPE). For the transdermal patch development, natural capsaicin (80mg) with 1.0mL of ethanol was dissolved in polymeric gels. The gels used were made from the polymers; hydroxypropyl methyl cellulose (HPMC), hydroxypropyl cellulose (HPC), methyl cellulose (MC), and Pluronic F-127 (15%). The release of capsaicin was studied using Distek dissolution apparatus with a modified method of dissolution. Results The pepper Cajun tobasco reported the highest amount of capsaicin in the accessions tested of 10.84 mg/gr of total capsaicinoids, followed by the ornamental Bolivian rainbow: 7.02 mg/gr of total capsaicinoids. For the initial characterization for capsaicin patch development, the relationship between the type of gel and elapsed time was plotted. It was noticed that MC gel released the greatest amount of capsaicin in a shorter period of time followed by HPC, HPMC, and then Pluronic F-127. HPLC analysis of the Franz diffusion cell revealed no permeation through the rat skin when using the MC and HPC. Conclusion The results of this study suggest that further research is needed for more polymer gels, including greater concentrations of current polymer gels, regarding the development of a patch for the transdermal delivery of capsaicin.
GM07  Microchannel Electrophoretic Analysis of Amyloid Protein Aggregation

Christa Hestekin, Ph.D.
Assistant Professor, University of Arkansas
chesteki@uark.edu

Amyloids are involved in a variety of diseases including Alzheimer’s Disease and diabetes. A number of technical challenges exist for the quantitative analysis of the different sizes of amyloid proteins which are present during the early stages of aggregation, therefore requiring new technologies to be developed for enhanced protein separations. Microchannel electrophoretic techniques have emerged as powerful tools for the quantitative analysis of proteins. In this study, we investigated the ability of capillary and microchip electrophoresis to monitor the early stages of amyloid aggregation using amyloid beta (Aβ) and amylin as a model amyloid-forming proteins. For the Aβ protein, sample preparation effected the size of the initial starting material as well and the rate of protein aggregation. In addition, electrophoretic conditions including the use of polymeric coating and separations matrices as well as aggregation conditions (agitation, salt, etc.) were determined to affect the rate of protein aggregation.

GM08  Telemedicine Collaboration Improves Perinatal Regionalization and Lowers Statewide Infant Mortality

Richard Whit Hall, M.D.
Professor, University of Arkansas for Medical Sciences
hallrichardw@uams.edu

Richard Whit Hall, Richard W. Hall, MD1, Elizabeth W. Kim, MD1 Terri J. Teague-Ross, MS2 William W. Greenfield, M.D.2 D. Keith Williams, Ph.D.3 Dennis Kuo, M.D.2 1Department of Pediatrics/Neonatology, College of Medicine, University of Arkansas for Medical Sciences and Arkansas Children’s Hospital, Little Rock, Arkansas 2Department of Obstetrics and Gynecology, Center for Distance Health, College of Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas 3Department of Biostatistics, University of Arkansas for Medical Sciences, Little Rock, Arkansas

OBJECTIVES: We assessed a telemedicine (TM) network’s effects on decreasing deliveries of very low birth-weight (VLBW, <1500 grams) neonates in hospitals without Neonatal Intensive Care Units (NICUs) and statewide infant mortality. STUDY DESIGN: This prospective study used obstetrical and neonatal interventions through TM consults, education, and census rounds with 9 hospitals from July 1, 2009 - March 31, 2010. Using a generalized linear model, Medicaid data compared VLBW birth sites, mortality, and morbidity before and after TM use. Arkansas Health Department data and chi square analysis were used to compare infant mortality. RESULTS: Deliveries of VLBW neonates in targeted hospitals decreased from 13.1% to 7.0% (p=0.0099); deliveries of VLBW neonates in remaining hospitals was unchanged. Mortality decreased in targeted hospitals (13.0% before TM and 6.7% after TM). Statewide infant mortality decreased from 8.5 to 7.0 per 1000 deliveries (p=0.043). CONCLUSIONS: TM decreased deliveries of VLBW neonates in hospitals without NICUs and was associated with decreased statewide infant mortality.
**GM09**  Effect of spacer arm length and ligand density on affinity membrane based separation

Vibha Bansal  
Assistant Professor, University of Puerto Rico at Cayey  
vibha.bansal@upr.edu

**Vibha Bansal, Ezio Fasoli, Dept. of Chemistry, Univ. of Puerto Rico at Humacao, PR.**

Despite membrane-based separations offering superior alternative to packed bed chromatographic processes, there has been a substantial lacuna in their actual application to separation processes. One of the major reasons behind this is the lack of availability of appropriately modified or end-group modifiable membranes. In this paper, an affinity membrane was developed using a commercially available serine protease inhibitor, para-aminobenzamidine (pABA). The membrane modification was optimized for protein binding capacity by varying: i) the length of the spacer arm (SA; 5-atoms, 7-atoms, and 14-atoms) linking the ligand to membrane surface; ii) the affinity ligand density on membrane surface (5-25 nmoles per cm2). Resulting membranes were tested for their ability to bind plasminogen activators (PAs) from mono- and multi-component systems in batch mode. The membrane containing pABA linked through 7-atoms SA but similar ligand density as in the case of 5- or 14-atoms long SA was found to bind up to 1.6-times higher amounts of PA per nmole of immobilized ligand from conditioned HeLa cell culture media. However, membranes with similar ligand densities but different lengths of SA, showed comparable binding capacities in monocomponent system. In addition, the length of SA did not affect the selectivity of the ligand for PA. A clear inverse linear correlation was observed between ligand density and binding capacity until the point of PA binding optima was reached (11±1.0 nmoles per cm2) in mono- and multi-component systems for 7- as well as 14- atoms SA. Up to 200-fold purification was achieved in a single step separation of PA from HeLa conditioned media using these affinity membranes. The issues of ligand leaching and reuse of the membranes were also investigated. An extensive regeneration procedure allowed the preservation of approximately 95% of the PA binding capacity of the membranes even after five cycles of use.

**GM10**  The effect of prenatal steroids on the fatigue resistance of the fetal guinea pig diaphragm

Jennifer L. Dearolf, Ph.D.  
Associate Professor, Hendrix College  
dearolf@hendrix.edu

**Jennifer L. Dearolf, Lance A. Riley and Rebekah A. Walker, Hendrix College**

The application of glucocorticoid steroids to women at risk of premature birth has increased the viability of their infants, but little is known about the effects of these steroids on the development of breathing muscles. We hypothesize that the administration of betamethasone, a glucocorticoid, during muscle fiber differentiation will increase the fatigue resistance of the diaphragm in fetal guinea pigs. To test this hypothesis, we removed diaphragms from fetal guinea pigs that were treated with two injections per week of betamethasone (0.5 mg/kg) or sterile water. These injections occurred twenty-four hours apart at 65%, 75%, and 85% gestation. We then measured the contractile abilities of the fetal diaphragms using a standard two-minute fatigue test and a tetanic force fatigue test. Results from the two-minute fatigue test demonstrated that exposure to prenatal steroids does not lead to a significant difference between the fatigue resistance of control and treated fetal diaphragms, while preliminary tetanic fatigue data showed that control diaphragms are slightly more fatigue resistant than treated diaphragms. However, when analyzing the contractile response of the diaphragm, we realized that no diaphragm (treated or control) reached tetanus during the standard two-minute fatigue test, which led to changes in our fatigue test protocol: the duration of the stimulation trains was extended and the time between trains was reduced. Using the revised fatigue test, results that support our hypothesis would indicate that a multi-course exposure to betamethasone leads to a more fatigue-resistant diaphragm. Therefore, treated premature infants may better sustain ventilation during times of stress than untreated infants.
Chemistry and biology of a resin-glycoside family of natural products – ipomoeassins

Wei Shi, Ph.D.
Assistant Professor, University of Arkansas - Fayetteville
weishi@uark.edu

Wei Shi, Guanghui Zong, University of Arkansas - Fayetteville
Eric Barber, University of Arkansas - Fayetteville

To better understand their mechanisms of action and facilitate future molecular design of new therapeutic agents with improved efficacy, bioactive natural molecules are widely used as tools to study biological systems. Isolated from the plant Ipomoea squamosa in Suriname, the ipomoeassins are a series of related macrolide resin glycosides with embedded disaccharide moieties. This family of natural glycoconjugates showed low nM cytotoxicity against several tumor cell lines [1,2]. Among them, ipomoeassin A showed selective anti-proliferation activity in the NCI 60-cell line screen. Its pattern of activity did not have significant correlation with any other known anticancer agents when subjected to COMPARE analysis [3], thus raising the possibility that the ipomoeassins have an entirely novel mechanism of action through new molecular targets. To facilitate future molecular design of new therapeutic agents derived from the ipomoeassins, our objective in this project is to identify, assess, and confirm cellular targets of the ipomoeassins by using synthetic chemistry, analytical biochemistry, and cell and molecular biology methods. We hypothesize that the ipomoeassin resin glycosides are suitable for interrogating novel therapeutic targets as underexplored chemical space. Our central technique is to synthesize photo-crosslinking activity-based probes (hvABPs) of the ipomoeassins for protein profiling to identify protein targets of these unique molecules. However, the total syntheses of the ipomoeassins have been accomplished just very recently. There is no sufficient SAR information available for rational design of ipomoeassin probes. Therefore, we report herein our research efforts towards new synthetic routes for easy access to ipomoeassin analogs with great structural variations. 1. Cao, S., R. C. Guza, et al. J. Nat. Prod. 2005, 68, 487-492. 2. Cao, S., A. Norris, et al. Nat. Prod. Res. 2007, 21, 872-876. 3. Kingston, D. G. I. J. Org. Chem. 2008, 73, 3975-3984.

Regulation of Musashi2-mediated mRNA translation in control of cell fate transitions

Melanie C. MacNicol, Ph.D.
Assistant Research Professor, University of Arkansas for Medical Science
macnicolmelanie@UAMS.edu

Melanie C. MacNicol, Ph.D., Center for Translational Neuroscience, University of Arkansas for Medical Science, Chad Cragle1,2, Lillian Shao3, Daohong Zhou3,4, Angus MacNicol4,5 1Department of Physiology and Biophysics, 2Center for Translational Neuroscience, 3Department of Pharmaceutical Sciences, 4Winthrop P. Rockefeller Cancer Institute, 5Department of Neurobiology and Developmental Sciences, University of Arkansas for Medical Sciences

Stem cell function is determined by cellular signaling mechanisms that drive cell fate transitions. The mechanisms underlying stem cell self-renewal versus cell differentiation are not fully understood. In this study, we demonstrate a role for targeted mRNA translation, mediated through the mRNA-binding protein Musashi2 in control of oocyte cell cycle progression. We show Musashi2 is modified through phosphorylation on two evolutionarily conserved sites in response to environmental differentiation stimuli. Musashi2 phosphorylation is mediated through two key cell cycle regulatory mechanisms; the cyclin-dependent kinase (CDK) and MAP kinase signaling pathways and results in translation of target mRNAs encoding cell cycle control proteins. A similar stimulus-dependent phosphorylation of the two conserved activating sites is observed after heterologous expression of mammalian Musashi2 in Xenopus oocytes. We further observe phosphorylation of endogenous Musashi2 in mammalian stem cells in response to growth control stimuli, coincident with cell differentiation. Our data indicate a conserved role for Musashi2-mediated mRNA translation in cell cycle control and suggest Musashi2 phosphorylation as a potential target for development of diagnostic markers or therapeutic interventions in control of stem cell function.
GM13  Crystal structure comparison and stability data study for apo and holo of Clostridial PKD-like domain

Katarzyna Janowska, Ph.D.
Post Doctoral Fellow, University of Arkansas
kjanowsk@uark.edu

Katarzyna Janowska, Ethan Latimer, University of Arkansas for Medical Sciences Little Rock, AR; Osamu Matsushita -Okayama Univ, Grad Sch Med, Dept Bacteriol Dent & Pharmaceut Sci, Okayama 7008530, Japan; Joshua Sakon UA Dep. Chemistry and Biochemistry

Clostridium histolyticum secrets two type of collagenase (ColH) and (ColG). Bacterial collagenases consist of multimodular domains. Starting from N-terminal the segments are: catalytic domain S1, polycystic kidney disease-like (PKD) domains (S2a and S2b in ColH; S2 in ColG), and collagen binding domain (S3 in ColH; S3a and S3b in ColG). In contrast to collagenolytic mechanism of mammalian matrix metalloproteases (MMPs) bacterial collagenases are much less sequence specific. Each domain in Clostridial collagenase is believed to play a unique role in collagenolysis (Fields, 2013 J Biol Chem 288, p.8785). Polycystic kidney disease (PKD) domain is 80-90 amino acids segment. Its presence in many surface layer proteins of archaebacteria (Jing, 1999 EMBO J., 18, p.297) and in many biopolymer hydrolases, such as chitinases, celluloses suggests that PKD play important role in biopolymer degradation (Orikoshi, 2005, J. Appl. Microbial. 99, p.551; Oda, 1996, J. Biochem., 120, p.564). The PKD-like domain has been shown to swell, but not unwind collagen (Wang, 2010 J Biol Chem 285, p.14285). The although Clostridial PKD-like domains do not bind tightly to collagen (Matsushita, 1998, J Biol Chem 273, p.3643), the domain has been shown to help the CBD bind stronger to collagen fibrils. Here we present X-ray crystal structures of PKD –like domain of collagenase H from Clostridium histolyticum with absence (apo) and presents of calcium ion (holo) determined at high resolution, 1.8 Å and 1.9 Å respectively. In holo structure, one Ca2+ is bound. Calcium plays significant role with enzymatic activity of collagenases as well as its stability (Bauer, 2013 J Bacteriol 195, p.318; Philominathan, 2009 FEBSJ 276, p.3589). Our thermal and chemical denaturation study of PKD-like domain demonstrated that Ca2+ stabilize the 3D structure.

GM14  Leading-Edge Protein and Genomic Services at the MUSC Proteogenomics Facility

Jeremy L. Barth, Ph.D.
Assistant Professor, Department of Regenerative Medicine and Cell Biology, Medical University of South Carolina
barthj@musc.edu

Jeremy L. Barth, Victor M. Fresco, Department of Regenerative Medicine and Cell Biology, Medical University of South Carolina Cynthia K. Gittinger, Department of Regenerative Medicine and Cell Biology, Medical University of South Carolina Waleed O. Twal, Department of Regenerative Medicine and Cell Biology, Medical University of South Carolina W. Scott Argraves, Department of Regenerative Medicine and Cell Biology, Medical University of South Carolina

The MUSC Proteogenomics Facility is an SCINBRE supported resource that provides regional investigators with expertise, instrumentation and turnkey services for a range of genomic and protein-related technologies. The Facility currently offers Genomics services that include 1) next-generation sequencing with the Ion Torrent PGM, 2) array-based transcriptomic profiling (mRNA, microRNA) and SNP genotyping analysis services with an Affymetrix platform, (3) RNA quality assessment with an Agilent Bioanalyzer, and 4) quantitative PCR analysis with a BioRad Cfx96. Protein-related services include 1) multiplex analysis of cytokines, phosphoproteins and microRNAs, and 2) biomolecular interaction analysis using a BIAcore 3000 surface plasmon resonance instrumentation. Bioinformatics services cover a full spectrum of microarray-related analyses, DNA sequence alignment and assembly, and training in online and stand-alone informatic software, statistical analysis, promoter and transcription factor analyses and bioinformatic tool development. Since the formation of our Facility in 2003, the Facility has steadily increased the number of services provided per year as well as the number of investigators assisted. In FY2012-13, our Facility assisted 60 investigators at SC institutions, including Clemson, The Citadel, Furman, MUSC, Presbyterian College, USC, SC State University, USC Beaufort and Winthrop, ageraging approximately 70 services/usages per month. This included the support of >23 grant applications, either through experiment planning, support letters, and/or participation as co-investigators. In addition to our technical services, the Facility also provides training and consultation, conducts outreach to institutions across South Carolina, and encourages students and faculty to tour the Facility. Detailed description of current services and fees can be found at the MUSC Proteogenomics Facility website, http://proteogenomics.musc.edu/.
GM15 The UMMC Molecular and Genomics Facility: Center for Psychiatric Neuroscience COBRE Core Component

Zibiao Guo, Ph.D.
Research Scientist, University of Mississippi Medical Center
mrgarrett@umc.edu

Zibiao Guo, Michael R. Garrett Department of Pharmacology and Molecular and Genomics Core Facility University of Mississippi Medical Center, Jackson, MS

The University of Mississippi Medical Center (UMMC) Molecular and Genomics Core Facility (MGCF) provides centralized access to molecular and genomics expertise and services for the University and external researchers. In recent years, it has become evident that a scientific approach using high-throughput genomic technologies, such as microarray and next-generation sequencing (NGS) can provide an enormous capacity to understand the complex interaction of biological systems associated with human health and disease. Mission: The mission of the MGCF is to serve as a nucleus to develop research and educational programs to increase the competitiveness and enhance biomedical discovery of researchers. Equipment: The MGCF is equipped with several genomics platforms, including Affymetrix 3000 7G and GeneAtlas Instruments for whole genome expression profiling and an Illumina MiSeq for small RNA sequencing (miRNA), ChiP-Seq, and amplicon sequencing. Mammalian level RNA-Seq services are offered by in-house preparation of libraries, quality control on MiSeq and deep-sequencing (Illumina HiSeq) using an outside service provider. Services: The MGCF provides the following services: (1) sample preparation, quality control, and storage; (2) sequencing and genotyping; (3) microarray, NGS, and validation via quantitative real-time PCR; (4) lentiviral methodologies; and (5) preliminary bioinformatics analysis. In summary, the MGCF supports investigators and enables the generation of hypothesis-driven ideas to develop new approaches to evaluate complex behavioral traits, study the effect of novel medicinal, pharmacological compounds controlling behavior or neurological processes, and to enhance the discovery of biomarkers in disease states. Supported by P30 GM103328 (CPN-COBRE) and P20 GM103476 (MS-INBRE).

GM16 Photoinduced Electron Transfer in the Rb. Sphaeroides Cytochrome bc1 Complex

Francis Millett, Ph.D.
Professor, University of Arkansas, Fayetteville
millett@uark.edu

Francis Millett, Jeffrey Havens1, Quan Yuan1, Shaoqing Yang2, Chang-An Yu2, Linda Yu2, Bill Durham1, 1Univ. Arkansas, Fayetteville, AR, 2Oklahoma State Univ., Stillwater, OK

Electron transfer within WT R. sphaeroides cytochrome bc1 was studied using a ruthenium dimer, Ru2D, to rapidly photo-oxidize heme c1 within 1µs. A range of different conditions including viscosity, temperature, inhibitors and substrates was used to study electron transfer between the iron-sulfur protein (ISP) and heme c1, as well as electron transfer through the b hemes following turnover. Electron transfer between the ISP and heme c1 was biphasic, with an initial fast rate, k1, of 80,000 s-1, and slow rate, k2, of 3,500 s-1. k1 was found to decrease significantly with increasing viscosity, suggesting that k1 is gated by rotational diffusion. k1 and k2 were fully inhibited by half an equivalent of the stigmatellin, indicating that both ISP were unable to rotate toward the c-state when stigmatellin is bound to only one Qo site of the monomer. Electron transfer through the b hemes following Qo site turnover was observed with an initial reductive phase with rate constant, k2, of 3,500 s-1, followed by a slower re-oxidation of heme bH with a rate constant, k4, of 500 s-1. Two equivalents of heme bH were re-oxidized per quinol oxidized at the Qo site. It is also shown that k4 is not affected by antimycin until at least half an equivalent of the inhibitor is present. This suggests that the quinone product of Qo site turnover diffuses through the hydrophobic interior of the complex to act as substrate at the Qi site, and that electrons are transferred across the hemes bL with a rate constant of at least 500 s-1. Supported by NIH grants GM20488 and 8P30GM103450.
GM17 Angiotensinogen is differentially regulated by angiotensin II and interleukin 6 in renal proximal tubular S1, S2 and S3 cells

Ryousuke Sato, Ph.D.
Instructor, Tulane University Hypertension and Renal Center of Excellence
rsato@tulane.edu

Ryousuke Sato, Kathleen S. Hering-Smith; Tulane University Hypertension and Renal Center of Excellence L. Lee Hamm; Tulane University Hypertension and Renal Center of Excellence L. Gabriel Navar; Tulane University Hypertension and Renal Center of Excellence

Intrarenal angiotensinogen (AGT) augmentation induced by angiotensin II (Ang II) and associated pathogenic factors including interleukin 6 (IL-6) cause further elevation of intratubular Ang II production, leading to the development of hypertension and kidney injury. Recent studies suggested that renal proximal tubular segments (S1, S2 and S3 segments) show different AGT expression levels under normal conditions. However, AGT expression and its regulation under Ang II and/or IL-6 stimulations in the segments have not been demonstrated. Thus, this study determined AGT levels and its response to Ang II and IL-6 in S1, S2 and S3 cell lines. Firstly, basal levels of AGT mRNA and protein, Ang II type 1 receptor (AT1R), NF-κB (a transcription factor in Ang II signaling pathways) and STAT3 (a transcription factor in IL-6 signaling pathway) were determined. In addition, the cells were incubated with 100 nM Ang II and/or 400 nM IL-6 for 24 h. Basal AGT levels in S1 and S3 cells were lower than in mouse whole kidney (0.09-fold and 0.33-fold compared with mouse whole kidney). S2 cells exhibited the highest basal AGT levels (4.15-fold) among these cells. Basal AT1R levels were lower in S3 than in S1 and S2 cells. Basal NF-κB levels were not different among the cells. Basal STAT3 levels in S3 cells were lower than that in S1 and S2 cells. In S1 cells, AGT expression was stimulated by IL-6 (1.89 ± 0.32, ratio to control) and co-stimulation with Ang II and IL-6 (1.85 ± 0.28) although Ang II alone did not alter AGT levels. In S2 cells, only the co-stimulation increased AGT expression (1.35 ± 0.01). No changes were observed by similar treatments in S3 cells. These results indicate that S2 cells are main source of intrarenal AGT which can be augmented by Ang II and IL-6 during the development of Ang II-dependent hypertension. Furthermore, low basal levels of AT1R and STAT3 in S3 cells explain why these cells do not respond to Ang II and IL-6.

GM18 Safety of Noninvasive Electrical Stimulation of Acupuncture Points (NESAP) during a routine heel stick

Charlotte C.Yates, PT,Ph.D., PCS
Associate Professor, Center for Translational Neuroscience, University of Arkansas for Medical Sciences
cyates@uca.edu

Charlotte C.Yates, PT,Ph.D., PCS, Anita Mitchell, Ph.D., APRN,University of Arkansas for Medical Sciences Leah Lowe, DPT, University of Central Arkansas Richard W. Hall, M.D., University of Arkansas for Medical Sciences

Objectives: To determine the safety of noninvasive electrical stimulation of acupuncture points (NESAP) in healthy term infants receiving routine heel sticks for metabolic screening. Design: A descriptive study was used to assess safety of a transcutaneous electrical nerve stimulation (TENS) unit to deliver NESAP to neonates. Setting/Subjects: Healthy term newborn infants less than three days old were enrolled before discharge from a hospital postpartum unit. Intervention: NESAP was administered to infants for 10 minutes prior to heel stick, for the duration of the heel stick and for 5 minutes afterwards. Self-adhesive electrodes were first applied to infants’ lower extremities at four acupuncture points, the TENS unit was connected and infants were continuously monitored for safety and comfort. Settings were gradually increased as the study progressed: the first six infants received 1.0 mA, 2 Hz; the second six infants received 2.0 mA, 10 Hz; and the last 18 infants received 3.5 mA, 10 Hz. Outcome Measures: Outcome measurements included: 1) skin assessment at electrode sites; 2) heart rate and rhythm, respiratory rate, oxygen saturation levels, and blood pressure; 3) pain scores using the Premature Infant Pain Profile (PIPP) and 4) functioning of monitors to assess for interference from TENS unit. Results: There were no significant changes in vital signs during and after NESAP. In the first 12 infants, there were no changes in PIPP scores after initiating the TENS unit. In the last 18 infants, some infants moved their legs for a few seconds, indicating that they probably felt the stimulation, with a slight increase in PIPP scores (from 2.65 to 3.5) for 30 to 90 seconds. There were no adverse events during or after NESAP. Conclusions: NESAP is safe for infants with low settings on TENS unit. Further research is needed to determine the effectiveness of the TENS unit to relieve pain in neonates during routine heel sticks.
A set of human conditions known as ribosomopathies are associated with haploinsufficiency for one of several ribosomal protein genes or other genes important for ribosome biogenesis. Clinical symptoms of ribosomopathies include anemia, bone marrow defects, skeletal defects and in some cases, increased risk of cancers. In Drosophila melanogaster (fruit fly), mutations in ribosomal protein genes results in a “Minute phenotype”. The Minute phenotype includes defects that are indicative of reduced protein synthesis such as delayed development, short and thin adult bristles and reduced fertility. However, similar to what is seen in human ribosomopathies, mutation of some Drosophila ribosomal protein genes also results in tumorous growths. To understand how disrupting ribosome biogenesis leads to cellular responses that cause developmental defects and tumor growth, we are studying the Drosophila Ribosomal Protein S6 (RpS6) gene which is a “dual gene” in that it codes for a ribosomal protein as well as a small non-coding RNA predicted to be a small nucleolar RNA (snoRNA). We are using a mutant allele of RpS6 called hen2. Heterozygous female flies (hen2/+) show a weak Minute phenotype in that they have a slight developmental delay. However, males have a quite different phenotype when they carry the hen2 allele of RpS6. These hen2/Y males have a prolonged larval period and die before adulthood. During larval development, hen2/Y males develop melanotic tumors, overgrowths of the larval hematopoetic organs. Because the first intron of the Drosophila RpS6 gene contains the information for a small non-coding RNA, mutations that reduce RpS6 expression also are expected to reduce expression of this small non-coding RNA. In this poster, we will present the results we have obtained in our work to the hypothesis that reduced expression of each component of the RpS6 “dual gene” makes distinct contributions to the phenotypes seen in hen2 flies.

Glycopeptide antibiotic vancomycin has been applied in the treatment of Methicillin Resistant Staphylococcus aureus strains. However, vancomycin intermediate strains of S. aureus (VISA) have been reported. The mechanism of vancomycin resistance is poorly understood. VISA strains are characterized by thick cell walls and decreased carboxypeptidase activity. In this study, we show that the msa locus plays a role in the regulation of vancomycin resistance in two VISA strains. An msa deletion mutant was created by allelic replacement method. Vancomycin susceptibility was measured by broth micro-dilution. Cell wall morphology was examined by transmission electron microscopy. For transcriptional analysis, qRT PCR was performed. Deletion of msa gene resulted in a significant decrease in the minimum inhibitory concentration (MIC) for vancomycin in both the strains. Growth curve in presence of vancomycin resulted in a decrease in the growth rate of the msa mutant. TEM analysis showed a significant decrease in the cell wall thickness in the msa mutant relative to wild type. Transcription profile of pbp4 showed that the msa mutant, unlike wild type, does not reduce expression of pbp4 in the presence of vancomycin. Down-regulation of pbp4 is a key factor in vancomycin resistance. These findings were confirmed by a fluorescent penicillin binding assay which showed that the msa mutant has a higher amount of Pbp4 protein relative to wild type. The msa locus is essential for vancomycin resistance in these VISA strains. Specifically, our results indicate that msa regulates the expression of pbp4, which in turn plays a key role in cell wall synthesis and mediates vancomycin resistance. Currently, we are investigating the amount of crosslinks in the cell wall of wild type and msa mutants by HPLC. This will allow defining the underlying mechanism for reduced vancomycin resistance in the msa mutant.
GM21 Processing Site Insertions To Examine Membrane Protein Translocation Into Thylakoid Membranes

LaRae Brown
Graduate Student, University of Arkansas
ldb002@uark.edu

LaRae Brown, Alicia Kight, Priyanka Sharma, and Ralph Henry, University of Arkansas

The light harvesting chlorophyll a/b binding proteins (the LHCs) are the most abundant membrane proteins in the world. LHCs are nuclear encoded proteins, which are targeted to the thylakoid membrane by a chloroplast signal recognition particle (cpSRP). Their Insertion into the thylakoid membranes is facilitated by a cpSRP receptor (cpFtsY) and a protein insertase (Alb3). Work here focused on understanding the molecular events of LHC insertion into thylakoid membranes using the cab80 gene product (LHCP) as a model. Specifically, we sought to develop a tool to detect membrane insertion of the lumen-localized loop of LHCP that would rely on cleavage of the loop by a thylakoid lumen processing protease. We also sought to understand effects of processing site insertion mutations on LHCP trimerization and assembly with photosystem II. Our data shows that insertion of the D1 processing site in the lumenal loop of LHCP functions as a tool to detect the integration of LHCP into the thylakoid membranes. Our data also shows that LHCP mutants containing the D1 or OE33 processing site in the lumenal loop are impaired in LHCP trimer assembly following insertion into thylakoid membranes. Interestingly, this mutation also prevents LHCP assembly into photosystem II. This slowed assembly of LHCP trimer and inhibited incorporation into photosystem II appears to be unique to the mutation at position 134 of full length LHCP.

GM22 Point-of-care Microelectronic Diagnostics For Early Phase Rickettsial Infections

Wenli Zhang
Graduate Student, Louisiana Tech University
wzh007@latech.edu

Wenli Zhang, Institute for Micromanufacturing, Biomedical Engineering Center, Louisiana Tech University, Adarsh Radadia, Institute for Micromanufacturing, Biomedical Engineering Center, Louisiana Tech University Scott Li, Biomedical Engineering Center, Louisiana Tech University Kevin Macaluso, Veterinary School of Medicine, Louisiana State University

"Miniaturized point-of-care diagnostics for Rickettsia at clinically relevant concentrations can help overcome time and labor needs of current methods and improve patient survival rates. Overall goal of this project is to develop a portable microfluidic biosensor that concentrates R. parkeri from serum using dielectrophoresis and antibody decorated electrodes, and electrically detects such concentration by impedance spectroscopy. We present results from our discrete efforts to dielectrophoretically preconcentrate Rickettsia and detect rickettsial presence via impedance spectroscopy down to 10^3 cells/ml. Our future work will explore coupling of dielectrophoresis and impedance biosensing to lower detection limit to 10 cells/ml.
Investigation of targeting and antioxidative properties of nanoparticles loaded by SOD and SOD mimetic

Kiseleva Raisa
Graduate Student, Clemson University
rkisele@g.clemson.edu

Kiseleva Raisa, Yun Xiang, Alexey Vertegel

Reactive oxygen species (ROS) generation is the main problem that accompanies many types of chronic inflammation processes, such as secondary spinal cord injury, stroke, heart attack and chronic obstructive pulmonary disease (COPD). There is a positive correlation between the levels of ROS production with the inflammation level. Excessive ROS production can lead to oxidative stress, damage of cellular structures and eventually to the cell death due to apoptosis. In a healthy environment, ROS levels are managed by antioxidant enzymes such as superoxide dismutase (SOD), catalase, glutathione peroxidase, as well as by small antioxidant molecules such as vitamin C, vitamin E, and glutathione. As an alternative for small antioxidant molecules, a number of SOD mimetic molecules were recently developed. However, use of these naturally derived and synthetic molecules for treatment of COPD is hindered by quick clearance of the therapeutic formulations by respiratory epithelium. Recently, biodegradable nanoparticles were shown to have several advantages for the targeted delivery of antioxidants, as they could be modified with specific antibodies and the drug could be loaded inside nanoparticles. In the present work we have studied the anti-oxidative properties of nanoparticles loaded either by SOD enzyme or by SOD mimetic molecules. We performed experiments with two different cell cultures: a mouse monocyte cell culture RAW264.7 (a model for inflammatory response) and normal human bronchial epithelial cells (a model for COPD). Oxidative stress was modeled in cell cultures by treatment with hydrogen peroxide and pro-inflammatory challenge was performed using lipopolysaccharides. Inflammation levels in cell cultures were assessed by measuring levels of interleukin-8 (IL-8) by ELISA and PCR methods. Targeting effect of antibody conjugated nanoparticles compare to the plain carrier of free drug was demonstrated in vitro using confocal fluorescent microscopy.

Investigation of three polymeric gels for the transdermal delivery of D-cycloserine for the treatment of anxiety disorders

Tammy Yoxtheimer
Graduate Student, University of Charleston School of Pharmacy
tammyyoxtheimer@ucwv.edu

Tammy Yoxtheimer, Hayley DeMay (University of Charleston School of Pharmacy), Anh Pham (University of Charleston), R. Griffith (West Virginia University), C. Sirbu (West Virginia University), Gagan Kaushal (University of Charleston)

Purpose: D-cycloserine (DCS), a partial N-Methyl-D-aspartate (NMDA) agonist, is an FDA approved drug for the treatment of tuberculosis and is only available in a 250 mg capsule. DCS is currently being used in at least 40 clinical trials as a treatment for different anxiety disorders at strengths from 50 to 200 mg. Based on our previous study, we have observed that DCS is sensitive to the acidic pH. Thus transdermal delivery of this drug might be a better option for the treatment of anxiety disorders. Transdermal delivery also increases compliance and DCS would bypass the first pass effect of drug metabolism where a great amount of drug is lost. The purpose of the present study is to characterize a suitable polymeric gel for the transdermal delivery of DCS. Methods: Release of DCS and viscosities of the gels at certain concentrations will define what gels are suitable to serve as a vehicle for this medication. Three different polymeric gels were prepared; hydroxypropyl methyl cellulose (HPMC), hydroxypropyl cellulose (HPC) and methyl cellulose; at concentrations of 0.5 to 4% w/v and examined to determine a relationship between their concentrations, viscosities, and dissolutions. Physical properties were measured and viscosities were calculated using the RheoCalc program with a Brookfield Rheometer. Results: After graphing the relationship between the concentration of the gels and their respective viscosities, it was noticed that HPMC has the greatest increase in viscosity, then MC, then HPC, relative to the same increases in concentrations. It was also noted that the viscosities of HPMC were much higher at lower concentrations than the viscosities of HPC and MC at higher concentrations. The release of DCS from these gels at the different concentrations was observed not to be dependent upon the viscosity. Conclusion: The results of this study provide the impetus for further research and trials regarding the development of DCS for transdermal delivery.
GM25  Structural and cross-linking studies of the bacterial collagenolytic mechanism

Ryan Bauer
Graduate Student, University of Arkansas-Fayetteville
rbauer@email.uark.edu

Ryan Bauer, Keisuke Tanaka1,2, Rohana Liyanage3, Jackson O Lay Jr3, Takehiko Mima4, Osamu Matsushita4, and Joshua Sakon1
1Department of Chemistry and Biochemistry, University of Arkansas 2Nippi inc., Research Institute of Biomatrix 3The Arkansas Statewide Mass Spectrometry Facility, University of Arkansas 4Faculty of Medicine, Okayama University

Bacteria secrete collagenases that are responsible for extensive tissue destruction. As opposed to mammalian matrix metalloproteases (MMPs) bacterial collagenases are much less sequence specific. Clostridium histolyticum secretes collagenases ColG and ColH that are segmental enzymes consisting of a catalytic domain and variable numbers of both polycystic kidney disease-like (PKD) domain, and collagen binding domain (CBD). The crystal structure of the catalytic domain of s1 from ColG has been solved and revealed an open conformation. The small angle X-ray scattering-derived structure of the ColH catalytic domain suggests that calcium induces a closed conformation. To elucidate the mechanism of the catalytic domain, structural studies of the catalytic domain from Clostridium limosum and Grimontia hollisae have been initiated. Crystallization conditions have been identified for each domain, though obtaining strongly diffracting single crystals remains a bottleneck. Meanwhile, the crystal structures of the CBD from ColH and one of the CBDs from ColG have also been reported. The CBDs closely resemble each other despite sharing 30% sequence identity. Three aromatic residues that are critical for collagen binding are conserved. The CBDs have been shown to extend activity of growth factors in vivo, and thus, are being studied as drug delivery vehicles. Fusion proteins consisting of growth factors, cytokines, or hormones have been fused to collagen binding segments that include CBD. Preclinical outcomes differ greatly depending on which collagen binding segment was used. In order to better understand the targeting mechanism of CBD, a serine near the binding pocket has been mutated to cysteine in order to covalently cross-link the CBD onto collagen so that its location can be mapped using mass spectrometry (LC-ESI-MS/MS). Putative binding sites have been identified.

GM26  The Role of Islet Transcription Factors in Endocrine Pancreas

Dominique Washington
Graduate Student, Louisiana State University in Shreveport
DCWashin014@yahoo.com

Dominique Washington, Dr. Michael S. Lan, Louisiana State University Health and Sciences Center-New Orleans

Differentiation of pancreatic endocrine cells depends on the activation of genes that are controlled by transcription factors. There has been various islet transcription factors (ITFs) contribute to the development of pancreas. Being able to understand the functional roles of ITFs during different stages in pancreatic development will be helpful to promote precursor cells or another cell type to trans-differentiate into islet-like cells that can be used as a therapeutic target for diabetes. In the present study, the TAT-fused ITFs were used to trans-differentiate acinar cells into insulin-positive cells. Protein transduction domains (PTDs) derived from HIV-TAT peptide were fused with each ITF, which allow the uptake of ITF protein into various cell types. Four TAT-fused ITFs, Ngn3, Pdx-1, MafA, and NeuroD1 were designed in a bacterial GST-His6-TAT recombinant protein expression system. The recombinant proteins were expressed with IPTG induction and purified to homogeneity. The biological activity from each ITF was attained by nuclear transduction, induction of target promoter activity and the trans-differentiation of pancreatic acinar cells into insulin-positive cells. This study will provide significant information for developing strategies using recombinant TAT-fused proteins instead of adenoviral vector for converting pancreatic cells into insulin-positive cells for the treatment of diabetes.
**GM27**  
Deletion of Leptin Receptors in Somatotropes Affects Neonatal Development and Metabolism, Leading to Adult-Onset Obesity

Melody Allensworth-James  
Graduate Student, University of Arkansas for Medical Sciences  
mallensworth@uams.edu

**Melody Allensworth-James, Angela Odle, Anessa Haney, Gwen Childs Department of Neurobiology and Developmental Sciences, Center for Translational Neuroscience, and University of Arkansas for Medical Sciences**

Leptin regulates appetite and energy expenditure, and may also regulate organogenesis and development. We investigated the effects of somatotrope specific leptin receptor (LEPR) deletion on neonatal development of growth hormone (GH) cells and metabolic activity in adults. After proving selective deletion of LEPR only in the pituitary, we studied neonates at pnd 1, 5, 10, 15, and 21. In adult (4 mo) mutants, the % immunolabeled GH cells and serum GH were reduced significantly. In contrast, neonate mutants had serum GH levels similar to those of controls, with highest levels on day 1 (111 ± 66 ng/ml control n=7; 98.6 ± 60 ng/ml mutants n=8) followed by a sharp reduction to 3.96 ± 2.9 ng/ml, controls and 5.6 ± 4.6 ng/ml, mutants by day 15. Control mice had a significant increase in % immunolabeled GH cells from 5-10d of age to 42-45% of pituitary cells. In contrast, mutant males showed reduced % GH cells (20-23%) and no increase with age, while mutant females showed a slight increase with age (14-28%, p<.007). A Comprehensive Laboratory Animal Monitoring System evaluated metabolic factors causing obesity. At 2.5- 4 months of age, pre-obese mutant males had significantly higher respiratory quotients (p<.034) and were less active in both dark and light cycles (p<.01). Mutants ate 21% more food/bout than controls during the dark cycle (p<.003), but not more food overall. Serum leptin was normal. Sleep analyses showed that mutants sleep 30% less overall (p<.032) and 37% less during the light phase (p<.019). qPCR assays show normal GH mRNA in mutants. In light of the normal mRNA and the decreased % immunolabeled GH cells, leptin may play a post-transcriptional role in expression of GH proteins. The lack of leptin signals results in GH deficiency with consequent metabolic problems and adult onset obesity. This points to an important pathway whereby leptin optimizes body composition. Supported by NIH1R01HD059056(GVC); NIHNCRRP20RR020146; NIHP30NS047546, NIHR03HD059066(GVC).

**GM28**  
Pituitary leptin, not adipocyte leptin, maintains somatotrope cell populations

Angela K. Odle  
Graduate Student, University of Arkansas for Medical Sciences  
akodle@uams.edu

**Angela K. Odle, Melody Allensworth-James, Anessa Haney, Noor Akhter, Gwen V. Childs Department of Neurobiology and Developmental Sciences, Center for Translational Neuroscience, University of Arkansas for Medical Sciences, Little Rock, AR**

Leptin is a cytokine produced primarily in adipose tissue, though the hormone is also made in the pituitary and other tissues. Our lab has previously shown that the leptin signal is important for the maintenance and output of growth hormone-producing cells (somatotropes). However, it was not clear whether adipocyte leptin or pituitary leptin was responsible for this maintenance. Therefore, we have created two animal models to determine which source of leptin is responsible for the maintenance of somatotropes and/or GH secretion. We have created two tissue-specific leptin knockout mouse models using floxed Lep exon 3 and either Cre-Adipoq (for deletion in adipocytes) or Cre-GHRHr (for deletion in somatotropes, lactotropes, and thyrotropes). Serum (for hormone EIAs) and pituitaries (for dispersed-cell immunolabeling) were collected from adult animals from both lines. As expected, Cre-GHRHr deletion males have decreased % of cells labeled for leptin (CTL 35±3%, DEL 6±2%, p<0.002). Cre-GHRHr deletion males also have a significantly lower % of somatotropes (CTL: 31±1%, DEL: 16±2, p<0.002) and decreased (but not significant) serum GH. Cre-Adipoq deletion males have an increased % of cells labeled for leptin (CTL: 35.3% ± 1.5%, DEL: 45.6% ± 3.2%, p<0.02). There is no difference in % of somatotropes between Cre-Adipoq deletion males and controls, despite the deletion males being obese (76.32g ± 3.8g N=5) and having low serum GH levels (370.5pg/mL ± 97.60, N=6). Using two new leptin KO models, we have shown that (1) pituitary leptin is sufficient to maintain numbers of somatotropes in the absence of adipocyte leptin, and (2) adipocyte leptin may be responsible, at least in part, for the normal secretion of GH. These results indicate that the pituitary is an important source of leptin that works in cooperation with adipocyte leptin to sustain hormonal output. Supported by NIH 1R01HD059056 (GVC); NIH NCRR P20 RR020146; NIH P30 NS047546, NIH R03 HD059066 (GVC).
GM29  Characterization of a gulonolactonase, the first enzyme involved in ascorbate biosynthesis localized in the chloroplast

Jessica P. Yactayo-Chang
Graduate Student, Arkansas Biosciences Institute
jessica.yactayochang@smail.astate.edu

Jessica P. Yactayo-Chang, Guillermo Trujillo-Lujan1, Keat H Teoh1, Gwendolyn Wilson1, and Argelia Lorence1,2 1Arkansas Biosciences Institute, and 2Department of Chemistry and Physics, Arkansas State University, P.O. Box 639, State University, AR, 72467, USA. Email: alorences@astate.edu

Vitamin C (L-ascorbic acid, AsA) is the most abundant water-soluble antioxidant in plants and animals. In plants AsA is synthesized via four pathways involving L-galactose, D-galacturonate, L-gulose, and myo-inositol as main precursors. The inositol route to AsA involves four enzymes: myo-inositol oxygenase, glucuronate reductase, gulonolactonase (GNL), and L-gulono-1,4-lactone oxidase. The first two enzymes have been already characterized by the Lorence Laboratory. To identify the third enzyme, we aligned gene sequences of well characterized GNLs from rat and bacteria to the Arabidopsis thaliana genome. This resulted in the identification of 18 candidate genes. One of them (At1g56500) is particularly interesting because it possesses a chloroplastic signal peptide. The chloroplast is the subcellular compartment with the highest AsA level and an active site for production of reactive oxygen species. We have confirmed the localization of the enzyme after purifying the protein and measuring activity in isolated chloroplasts. Homozygous knockout lines in this gene have lower foliar AsA content compared to wild type (WT) controls, and displayed stunted growth, and chlorotic lesions, indicating the involvement of this enzyme in AsA synthesis and in maintaining a healthy redox balance in the leaves. Constitutive expression of At1g56500 in WT and the knockouts lead to lines with elevated AsA content. We are currently characterizing the phenotype of the knockouts, over-expressers, and rescued lines with a powerful phenomics tools (Scanalyzer HT). This instrument is equipped with visible, fluorescence, near infrared, and laser cameras that empowers unbiased, non-invasive, automated, and effective screening of plant phenotypes, particularly of small plants. In this poster we will present our progress in this work.

GM30  Link Between Vitamin C Content and Cold Tolerance in Rice

Sonia Elizabeth Castillo Gonzalez
Graduate Student, Arkansas Biosciences Institute, Arkansas State University
sonia.castillo@smail.astate.edu

Sonia Elizabeth Castillo Gonzalez, Katherine A Lisko1 Wen Gui Yan2 Anna McClung2 Argelia Lorence1,3 1Arkansas Biosciences Institute, Arkansas State University 2USDA-ARS Dale Bumpers National Rice Research Center 3Department of Chemistry and Physics

Rice is a staple food crop for half of the world’s population. Cold stress affects plant growth and crop productivity, causing rice production losses of more than 50% in East and Southeast Asia, Australia, Brazil, and the USA. In these regions, rice losses caused by cold stress are becoming more common due to climate change. Our ongoing project is a collaborative effort between the Lorence Laboratory at Arkansas State University, and the USDA-ARS Dale Bumpers National Rice Research Center as part of the NSF funded project from Sue Wessler’s Laboratory at UC-Riverside. As part of this project a mapping population was developed by crossing the line HEG4, which possesses multiple copies of the mPing transposable element, and the Nipponbare cultivar. This population was screened for cold tolerance at germination and lines with striking differences in their ability to germinate after continuous exposure to 12°C were identified. Cold tolerance is a complex trait that involves multiple mechanisms. A literature review on this subject indicates that high sugar and antioxidant content are linked to cold tolerance in rice. The Lorence Laboratory has previously demonstrated that Arabidopsis lines with elevated vitamin C (ascorbic acid, AsA) content are tolerant to cold stress. We hypothesize that in rice cold tolerance is also associated to a high AsA content. To test this hypothesis we are evaluating reduced, oxidized, and total vitamin C content in a subset of the population expressing extreme phenotypes (2 parents, one cold tolerant and one cold sensitive, plus 10 lines that displayed high and low cold tolerance). We are comparing the response of these lines to normal conditions (30°C) versus cold (12°C) stress at the vegetative stage 4 (V4), a stage of development where AsA accumulation peaks in rice. In this poster we will present our most recent findings on this subject.
GM32  The Scanalyzer HTS, a powerful phenomics tool to identify salt tolerance lines within a rice diversity panel

William Blair
Undergraduate Student, Arkansas State University
alorence@astate.edu

William Blair, Zachary Campbell1, William Blair1, Nykole De Vito1, Kayla Parker1, Malachy Campbell2, Harkamal Walia2 and Argelia Lorence1,3 1Arkansas Biosciences Institute, Arkansas State University, 2University of Nebraska, Lincoln, NE, USA 3Department of Chemistry and Physics, Arkansas State University, P.O. Box 639, State University, AR 72467, USA

Rice is arguably the most important crop for global food security, but is also the most salt-sensitive among staple cereals. Despite significant yield losses, rice is a good candidate for cultivation in areas prone to coastal flooding due to its ability to tolerate standing water in the field for long periods. These areas are also more prone to the effects of future climatic change. Therefore, there is an urgent need to harness the genetic potential of rice for salinity tolerance. The extent of genetic variation for salt tolerance in rice is largely unknown and under-utilized. Reasons for this knowledge gap had been lack of a tractable rice diversity panel with matching genomic resources, and the inability to precisely phenotype salinity stress responses over time in a high-throughput manner. This work is a collaborative effort between the Walia Laboratory at the University of Nebraska and the Lorence Group at Arkansas State University funded by the NSF Plant Genome Program. The Walia team has been studying the salt tolerance of a rice diversity panel at two developmental stages that are particularly susceptible to this stress in greenhouse experiments. Based on their results, a selected group of rice lines including salt tolerant and salt sensitive types as well as positive and negative controls was sent to the Lorence team to study their response to salt stress at the early vegetative growth stage using a high throughput phenotyping system called Scanalyzer HTS. This powerful platform available at the ASU-Jonesboro campus allows non-destructive measurement of plant size, architecture, chlorophyll and water content and other indicators of plant stress, such as leaf yellowing or chlorosis. In this work, we will present our progress in developing robust protocols for the identification and characterization of salt tolerant rice lines.

GM33  Effect of prenatal steroids on the myoglobin concentration in fetal guinea pig rectus abdominis muscles

Anvesh Kompelli
Undergraduate Student, Hendrix College
kompelliar@hendrix.edu

Anvesh Kompelli, Jennifer Dearolf, Hendrix College

Currently, glucocorticoids are used to promote the survival of premature children by accelerating their lung development. However, very little is known presently about how these steroids affect breathing muscle development. Work in our laboratory has shown that one of these steroids, betamethasone, increases the concentration of NADH-D, an oxidative enzyme, in an accessory inspiratory muscle of guinea pigs. These results suggest prenatal glucocorticoids accelerate the acquisition of mitochondria by fetal muscle, and to support the generation of ATP by these organelles, the fetal muscle would therefore require more oxygen. Thus, we propose that glucocorticoids will increase the concentration of myoglobin (Mb), the oxygen carrier in muscles, in a breathing muscle of fetal guinea pigs, the rectus abdominis (RA). To test this hypothesis, pregnant guinea pigs were given three injections of betamethasone (0.5 mg/kg) at 65%, 75% and 85% gestation. Twenty-four hours after the last injection, the females and their fetuses were euthanized and fetal tissue was collected. Extracts of the fetal muscle samples were prepared and separated in SDS-polyacrylamide (12%) gels for ~ 2 hours (30 mA/gel) at 18° C. These gels were silver stained, and ImageJ software was used to determine the proportion of Mb relative to actin in the treated and control RA muscles. If Mb concentrations are higher in the treated muscles, they may be better able to deliver oxygen to their mitochondria and thereby resist fatigue in comparison to non-treated muscles. Thus, babies exposed to prenatal steroids will have more mature breathing muscles and be better prepared to sustain their breathing during ventilatory challenges.
GM34 High Fat Diet and Predisposition to Endometriosis

Sarah Carr
Undergraduate Student, Ouachita Baptist University, Arkansas
carr49989@obu.edu

Sarah Carr, Ouachita Baptist University, Sarah Carr, Ouachita Baptist University, Melissa Heard, University of Arkansas for Medical Sciences (Physiology & Biophysics) Rosalia C.M. Simmen, University of Arkansas for Medical Sciences (Physiology & Biophysics and Pediatrics)

Endometriosis is a disease defined by the presence of endometrium fragments outside the uterus. It affects 7-10% of women and is associated with pain and infertility. The cause of endometriosis is unclear but it is suggested that an inflammatory environment, which can be caused by obesity, can increase predisposition to the disease. This study tests the hypothesis that a high fat diet alters the endometrium leading to increased predisposition to endometriosis. This study also examines how ectopic lesions caused by a defective uterus due to loss of expression of Kruppel-like factor 9 transcription factor may influence the eutopic endometrium. Ectopic lesions may negatively affect the eutopic uterus leading to infertility in women with endometriosis. Our laboratory has an established mouse model of endometriosis. To address the hypotheses I compared the proliferation status and expression levels of genes known to be dys-regulated in endometriosis in the endometria of mice fed a high fat diet with those of mice fed a control diet and compared the endometria of mice with wild type lesions with those of mice with KLF9 knockout lesions. Expression of genes related to endometriosis, inflammation, and cell proliferation were analyzed by quantitative RT-PCR. Immunohistochemistry was used to determine levels of Ki67 protein, a marker for cell proliferation, in uterine sections. Increased proliferation indicates enhanced estrogen signaling so more Ki67 should indicate a higher risk of endometriosis. Estrogen and progesterone levels in mice sera were evaluated to determine if high fat diet increases levels of circulating estrogens relative to progesterone, which may intensify lesion development. Levels of tumor necrosis factor alpha, a cytokine related to inflammation, were measured in the peritoneal fluid. Together this data will provide support for or against the contribution of a high fat diet to risk for endometriosis and the effect of ectopic lesions on the eutopic uterus.

GM35 Selection of fatty acid desaturase 7 (fad7-1) single mutant plants in Arabidopsis thaliana using SNP-PCR primers

Kaleb L. Vaughn
Undergraduate Student, Harding University
kvaughn1@harding.edu

Kaleb L Vaughn, Fiona L. Goggin Carlos A. Avila Carmen Padilla

Loss of function of the FATTY ACID DESATURASE7 (FAD7) has been reported to enhance plant defenses against aphids via enhanced levels of salicylic acid, a basal defense signaling hormone. The fad7-1 gene, a single nucleotide mutation, causes loss of function of FAD7. However the fad7-1 gene has a background of a glabra 1 (GL1) mutation in the model plant Arabidopsis thaliana, the gene associated with trichome formation. The absence of trichomes has been shown to cause defective systemic acquired resistance (SAR) in Arabidopsis. Any study of the FAD7 mutation with the GL1 mutant background in Arabidopsis may be called into question because the effect of the GL1 mutation is unknown. This calls for the isolation of the fad7-1 gene from the GL1 mutation in Arabidopsis. The methodology we used includes the use of allele-specific primers previously designed in lab to target specific alleles using variations of TD-PCR to maintain specificity in the binding of the primers. Because of availability, fad7-1/gl-1 plants were crossed with salicylic acid (SID2) mutants, but the SID2 mutants were screened out with SID2 wild-type allele specific primers after homozygous fad7-1 plants were identified using prodigy tests. By process of elimination using TD-PCR screening with allele-specific primers, phenotypic selection for the GL1 gene, along with using an inexpensive DNA extraction technique to verify line genotypes, a line of exclusively homozygous FAD7 Arabidopsis mutants has been identified. This experiment produces a line of homozygous fad7-1 mutant Arabidopsis that will be valuable for future experimentation, along with producing a better, inexpensive, and faster way to genotype plants.
GM36 Photocatalysed [4+2] Annulation of N-Cyclobutylanilines with Alkynes

Jean de Dieu Nubundiho
Undergraduate Student, Philander Smith College
jadookay@yahoo.fr

Jean de Dieu Nubundiho, Jiang Wang, Dr. Nan Zheng, University of Arkansas

The organic reactions mediated by visible light, a clean and inexpensive energy that cannot be used up, have increasingly received attention from the chemistry community. During the past five years, a number of organic reactions have been developed using visible light photoredox catalysis. In 2012, Dr. Zheng’s lab developed the photocatalysed [3+2] annulation of cyclopropylanilines with alkynes. We became interested in developing an analogous [4+2] annulation of N-cyclobutylanilines with alkynes because cyclobutanes have been almost neglected until recently. Some exciting chemistry involving cyclobutanes has been reported using Lewis acids or transition metals but not photocatalysts. To examine the proposed [4+2] annulation reaction, we needed to synthesize 6-(benzyloxy)-N-phenyl-1,2-dihydrocyclobutabenzen-1-amine as our starting material that took seven steps to prepare from resorcinol. Herein we present the [4+2] annulation of N-cyclobutylaniline with alkynes under visible light photocatalysis.

GM37 A Mass Spectrometry Signal-Enhanced Method for Metabolomic Measurements with Extremely Small Samples

Kyle M. Preston
Undergraduate Student, University of Central Arkansas
bmarquis@uca.edu

Kyle M. Preston, J. Alex Watts, and Bryce J. Marquis University of Central Arkansas, Chemistry Department

The field of metabolomics, the study of molecular fluxes associated with metabolism, is widely used to study a broad range of biological processes. In such studies the most popular measurement techniques for identification and quantification of metabolites feature chromatography combined with mass spectrometry detection. However, mass spectrometry is an insensitive measurement technique for a number of important metabolites that feature carboxylic acid and aldehyde functional groups (e.g., TCA cycle intermediates) due to the poor ionization of these groups. This decreased sensitivity requires large samples which in turn increases experimental costs and prevents metabolomic analysis in sample-limited studies. In order to overcome this limitation, we have developed novel methods for metabolomics featuring new derivatization techniques aimed to enhance the mass spectrometry signals of these key metabolites. In our study, liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) was optimized to detect both labeled and unlabeled TCA intermediates. The enhancements from two recently developed derivatization reagents were compared: 4-(2-(Trimethylammonio)ethoxy)benzenaminium dibromide (4-APBDA), and N-methyl-2-phenylethanamine (MPEA). TCA intermediates where quantified using isotope-labeled standard addition and the limits of detection were compared between labeled and unlabeled metabolites. The new methods were found to increase sensitivity more than 100 fold. Derivatized metabolite limits of detection were found to be on the order of 10-50 femtograms. This method was subsequently applied to quantification of metabolites from the nematode model organism C. elegans. The use of derivatization agents enabled quantification of both excreted and internal metabolites with sufficient sensitivity for metabolomics measurements to be taken from individual nematodes, measurements that are not possible with traditional methods.
GM38 Dissolution properties of goldenseal capsules

Leonce Nshuti
Undergraduate Student, Sewanee: The University of the South
nshuti0@sewanee.edu

Leonce Nshuti, Lin Song, Howard Hendrickson University of Arkansas for Medical Sciences, Department of Pharmaceutical Sciences

Goldenseal is one of the more popular supplements and has long been used to treat different diseases from infectious diarrhea to boosting the immune system. But these clinical results are unpredictable due in part to poorly characterized product. As part of the standardization of goldenseal capsules, steps were taken to develop an assay to study the dissolution by using an in vitro medium, which mimics the conditions in the human gastrointestinal tract. In this experiment a dissolution study of goldenseal capsules was done in order to determine the consistency in releasing major alkaloids of goldenseal from different batches of capsules. Prior to the dissolution test, the dissolution instrument was standardized using a prednisone validation test approved by the United States Pharmacopoeia (USP). The standardization of the prednisone method test was performed in UDT-804 universal dissolution apparatus, (Logan Instrument Brand, NJ) in a water medium at 37°C±0.5°C with a rotation speed of 50rpm. Both the first and the second stage of the standardization did not meet the USP standards but results of the second stage were on the margin. It was concluded that the apparatus could be used to study the dissolution of goldenseal. The dissolution study was done using three goldenseal capsule batches: 2003 CR (crushed roots), 2004CL (crushed leaves) and 2007M (mixture). The above batches were studied to determine the amount of Berberine, Hydrastine, and Canadine that dissolve after 30 minutes in a dissolution medium pH of 1.3 at 37°C with paddles rotating at a speed of 50rpm. The dissolution of these alkaloids pH-dependent and general followed the expected effects of pH on the ionization state of the tertiary amine in hydrastine and canadine. Dissolution of the quaternary ammonium compound berberine was more complex. These results establish dissolution parameters that can be used in the quality assessment of other Goldenseal products.

GM39 Piecing together the extraordinary DNA repair system of bdelloid rotifers

Nicholas P. Gill
Undergraduate Student, Hendrix College
gillNP@hendrix.edu

Nicholas P. Gill, James M. Williams, Hendrix College Andrew M. Schurko, Hendrix College

Bdelloid rotifers are aquatic, microscopic invertebrates comprised solely of females that reproduce asexually. Bdelloids have the unprecedented ability to recover from genome-wide DNA damage (e.g. double strand breaks) induced by high levels of ionizing radiation. This remarkable capacity for genome-wide DNA repair likely evolved as an adaptation for surviving desiccation and DNA damage. However, the molecular machinery used to repair damaged DNA in bdelloids is unknown. The objective of our research is to identify genes involved in this extraordinary DNA repair system. We are focusing on two groups of candidate DNA repair genes: meiotic genes and histone H2A variants. First, despite the lack of meiosis in bdelloids, their genomes contain several genes (e.g. SPO11, MSH4, MSH5, HOP1) that are specific to meiosis (and function during meiotic recombination) in other eukaryotes. Second, bdelloids have three histone H2A variants that are unique to this lineage, and represent intriguing candidates for involvement in DNA repair. We will test the hypothesis that meiotic genes and histone H2A variants are involved in DNA repair in bdelloids by using real-time PCR to quantify expression levels of these genes during recovery from DNA damage. Cultures of the bdelloid Adineta vaga will be desiccated (to induce DNA damage) and rehydrated (to initiate DNA repair). The upregulation of genes encoding meiotic proteins and H2A variants during rehydration (DNA repair) may suggest that these genes are maintained in bdelloids because they are involved in the DNA damage response. This research will lead to future investigations of other genes involved in the bdelloid DNA damage response, and pave the way for further studies on protein expression and interactions during DNA repair in bdelloids.
GM40

Developing RNAi to evaluate candidate DNA repair genes in bdelloid rotifers

Youmna Moufarrej
Undergraduate Student, Hendrix College
MoufarrejYE@hendrix.edu

Bdelloid rotifers are asexual microinvertebrates with resistance to DNA damage that is unprecedented among animals. Following high doses of ionizing radiation, DNA damage is efficiently repaired without loss of viability. This extraordinary DNA repair system is likely an evolutionary adaptation for surviving DNA damage incurred during desiccation. Bdelloids, therefore, provide a model for studying genes involved in DNA repair. We have identified two groups of genes that are candidates for involvement in DNA repair. First, bdelloid-specific histone H2A variants are unique in that they contain long C-terminal tails that might represent an adaptation for surviving desiccation-induced DNA damage. Second, although bdelloids lack meiosis, their genomes contain homologs of genes (e.g. SPO11, MSH4, MSH5) that are specific to meiosis (in particular, meiotic recombination and DNA repair) in model eukaryotes. The objective of this project is to analyze the function of bdelloid-specific H2A variants and meiotic gene homologs by developing a protocol for RNA interference (RNAi) in bdelloids. We evaluated two methods for inducing RNAi. For the “soaking method,” double-stranded RNA (dsRNA) that corresponds to a bdelloid transcript was introduced to bdelloid eggs/hatchlings using transfection solution. Transfection was monitored microscopically by observing uptake of fluorescein-labeled dsRNA. For the “feeding method,” we constructed a strain of E. coli HT115(DE3) that expresses a dsRNA copy of a bdelloid gene when induced with IPTG. Induced transformants were fed to A. vaga to induce RNAi.

GM41

In-Vivo Comparative Study of Metal Complexes in Amelioration of Toxic kidney Injury

Khatiana R. Butler
Undergraduate Student, University of Arkansas at Pine Bluff
wangilag@uapb.edu

Khatiana R. Butler, Khatiana R. Butler1; Nicholas Braman2; Richard B. Walker1; Richard B. Walker1; Alexei G. Basnakian2 and Grant W. Wangila1 1Department of Chemistry and Physics, University of Arkansas at Pine Bluff, Pine Bluff, AR  71601
2Department of Pharmacology and Toxicology, University of Arkansas for Medical Sciences, Little Rock, AR 72321

Background and Objective: It has been shown that metals have cytoprotective activity by stimulating antioxidant enzymes and inhibiting apoptotic enzymes. Zinc or copper combined with an antioxidant ligand has even greater cytoprotective effects. Studies show that zinc and copper complexes of amino thiols and salicylates have better cytoprotective activity than either metal or ligand. Both in vivo and in vitro data collected in this study strongly indicate that these metal complexes satisfy many of the criteria for prevention and treatment of kidney injury, as they are active, stable, and nontoxic antioxidants. Methods and Results: The study started with synthesis of the news zinc and copper compounds, characterization by elemental analysis and spectrochemical methods, followed by antioxidant activity using ABTS assay (zinc compounds) and NBT assay copper compounds) and in vivo toxicity studies. The compounds with lower IC50 and less toxicity in vitro were further studied in vivo. The animal study involved the elaboration of the model to ensure that the used dose of cisplatin induces kidney injury did not induce animal death. The mice were euthanized 96 h after cisplatin injection (IP, 20 mg/mg), and blood and kidneys were collected. The compounds were also tested in another model of acute kidney injury, rhabdomyolysis model induced by intramuscular glycerol injection (50% solution, 8 ml/kg). In both models our endpoints included: serum blood urea nitrogen (BUN) and creatinine to measure kidney function, and H&E histology to assess structural injury to the kidney. Conclusions and Discussion: Zn-RibCys exhibits strong protection in the Rhabdo model, but not in Cisplatin model. Cu-DIPS appear to be mildly protective in the rhabdo model, but not the Cisplatin model. In an interesting twist, Cu-DBS and Cu-DCS exhibit strong protection in the Cisplatin model, but none whatsoever in the rhabdo model.
GM42  Application of Computational Docking to Examine Metabolism of Chiral Drugs by CYP2C9

Timothy M. Horton
Undergraduate Student, Ouachita Baptist University, Arkansas
hor46650@obu.edu

Timothy M. Horton, (1) Grover P. Miller (2) Martin D. Perry, Jr. (1) Department of Chemistry, Ouachita Baptist University, Arkadelphia, AR, USA (2) Department of Biochemistry and Molecular Biology, University of Arkansas for Medical Sciences, Little Rock, AR, USA

Chiral drugs make up some 50% of drugs currently on the market. Frequently, chiral drugs are cleared much more favorably in one configuration than in the other. The motivation behind such selective metabolism is thought to be the arrangement of amino acids within the protein interior. Due to their nature and position in the channel in which oxidation occurs, certain residues could act to steer metabolism based on the drug’s stereochemistry. Computational approaches including molecular dynamics were performed to simulate the first step of an oxidation reaction. A novel approach involved the use of the Lennard-Jones potential to estimate the stabilizing energy afforded by each residue to the enzyme-ligand complex. The residues with the largest difference in energy between preferred configuration of the drug and non-preferred configuration were identified for eight chiral drugs.

GM43  A genetic approach to discern the roles of Drosophila ribosomal protein S6 and a potential snoRNA in growth defects

Shana Chancellor
Undergraduate Student, University of Arkansas at Monticello
stewartm@uamont.edu

Shana Chancellor, Hope Dunlap (UAM), Robert Rose (UAM), Helen Beneš (UAMS), Mary Stewart (UAM)

Many human disease genes are conserved with genes in Drosophila melanogaster (fruit fly), including those that cause a set of human conditions called ribosomopathies. Some human ribosomopathies are caused by mutation of ribosomal protein genes or other genes important for ribosome biogenesis. In Drosophila, mutation of ribosomal protein genes causes abnormalities such as delayed development, small adult size, reduced fertility, abnormal adult bristles and in a few cases, tumorous growth. Because Drosophila is a valid model for understanding human disease and is easily manipulated, we are studying the X-linked ribosomal protein S6 (RpS6) gene in Drosophila. The Drosophila RpS6 gene is actually a “dual gene” in that it codes for a ribosomal protein as well as a small non-coding RNA called Oraca2 that is predicted to be a small nucleolar RNA (snoRNA). In a mutant strain of flies called hen2, a transposon insertion in the promoter of the RpS6 gene causes reduced levels of RpS6 mRNA. Since expression of intron-housed RNAs is dependent on transcription of their host gene (RpS6 in this case), we expect that Oraca2 expression is affected by the hen2 mutation as well. Females that are heterozygous for the hen2 allele (hen2/+ females) develop into adults after a developmental delay, which is characteristic for mutations in Drosophila ribosomal protein genes. Male flies that are hemizygous for hen2 (hen2/Y males) show a more complex set of defects. The hen2/Y males have delayed development, develop tumorous hematopoetic organs and die before adulthood. In this poster, will present work with a set of transgenes that we are using to genetically dissect the contributions that disruption of RpS6 expression versus disruption of Oraca2 expression make to the defects observed in hen2 flies.
**GM44  Alkylation of Azole Derivatives**

Erin Jeffrey  
Undergraduate Student, University of Arkansas, Fayetteville  
ejeffrey@uark.edu

**Erin Jeffrey, Dr. Matt McIntosh, Sefat Alwarsh, and Maha Shrestha**

Azoles are 5-membered ring heterocycles containing a nitrogen atom and at least one other non-carbon atom. Azole derivatives are found in medicines that treat fungal infections, AIDS, cancer, and acid reflux disease, among others. The synthesis of these derivatives is a key step in acquiring the natural products used in these drugs. Forming C-C bonds at C2 of azoles is necessary in the current synthesis method which generally requires using strong bases, low temperatures, and/or expensive and toxic precious metal catalysts. Strong bases necessitate the use of protecting groups, which adds 2 steps to any synthesis and the use of extra materials. Low temperature requires the use of cryogens, a type of refrigerant, and must be carefully monitored to prevent exotherms which could potentially be dangerous to those near the reaction. The goal of this project is to develop a green, all-organic means of azole alkylation which will be useful for production scale synthesis.

**GM45  Interactions of histones H2A, H3 and H4 required for proper chromosome segregation during cell division**

Zach Reed  
Undergraduate Student, University of Arkansas at Little Rock  
zgreed@ualr.edu

**Zach Reed, Ines Pinto, Ph.D, University of Arkansas Fayetteville**

Histones are essential proteins involved in the compaction of DNA into chromatin. Histones play a role in all aspects of chromosome function, including transcription, DNA replication, repair, and chromosome segregation. The focus of this project is to analyze histone interactions with regards to chromosome segregation during mitosis, using the yeast Saccharomyces cerevisiae as a model organism. It has been found that specific histone H3 and H4 mutants cause chromosome mis-segregation during cell division. Based on the nucleosome location of the mutated amino acids and additional genetic evidence, we hypothesize that this segregation error is a result of the H3 and H4 mutants blocking the phosphorylation of serine 121 (S121) by Bub1 kinase in histone H2A. This phosphorylation is required for the recruitment of the protein shugoshin, which ensures proper microtubule attachment and chromosome segregation. To test our hypothesis, H2A S121 was mutated to glutamic acid and aspartic acid, which mimic phosphorylation. Both of these are predicted to suppress the chromosome segregation defects caused by the H3 and H4 mutants, while alanine will serve as a control since it cannot be phosphorylated. The S. cerevisiae strains to be tested will contain a deletion of one copy of the H2A-H2B genes and one copy carrying the mutated H2A S121 integrated at its chromosomal locus, along with the proper H3 and H4 mutations. These studies will help to shed light on the contribution that chromatin plays in establishing normal chromosome-spindle attachment during mitosis. In addition, they will increase our overall understanding of the molecular mechanisms underlying genetic disorders associated with chromosome mis-segregation, such as trisomies and cancer.
Infectious Disease/Immunology

ID11 Membrane Interactions and Biological Activities of Modified Antimicrobial Lactoferricin Peptides
Denise Greathouse, Ph.D.
Research Associate Professor, University of Arkansas, Fayetteville
dgreatho@uark.edu

Denise Greathouse, Colby Smith and Colton Kordsmeier, University of Arkansas, Fayetteville, Arkansas Tod D. Romo, Joshua N. Horn, and Alan Grossfield, University of Rochester Medical School, Rochester, NY

Pathogenic microorganisms are increasingly resistant to antibiotics, leading to a demand for new drugs. Modifications to LfB6 (RRWQWR-NH2), a hexapeptide, with broad spectrum antimicrobial properties, that enhance antimicrobial activity include: 1) sequence reversal (Retro LfB6: RWQWRR-NH2), 2) amino-acylation (CH3(CH2)nCO-), and 3) tryptophan-methylation (MeTrp). A designed heptapeptide with four arginines and two methyl-tryptophans (RRMeWQMeWRR-NH2; LfB7 MeTrp 3,5) further increases activity. The importance of backbone flexibility for activity and membrane interactions has been explored by changing the central glutamine of the heptapeptide to Gly or Pro. The membrane interactions and biological activities of the peptides were investigated by solid-state 2H and 31P NMR, fluorescence and circular dichroism spectroscopy, partitioning assays, fluorescence microscopy, and molecular dynamics (MD) simulations. Selective deuteration of the MeTrp residues allows the membrane interactions of the peptides to be examined by 2H NMR in oriented bilayers of mammalian- and bacterial-like membranes. The 2H NMR spectra reveal the MeTrp residues of the LfB peptides are aligned at the membrane surface, while 31P NMR spectra indicate the peptides induce little perturbation to the lipids. Membrane partitioning assays demonstrate peptide binding correlates with percent anionic lipid and N-acylation. Trp emission fluorescence spectroscopy shows the tryptophan residues are more water exposed in neutral compared to anionic lipid membranes. MD simulations confirm these findings, showing that while the non-acylated peptide comes on and off the neutral lipid during the simulation, the acylated peptide remains bound. Fluorescence microscopy with FITC-LfB6 shows that the peptide translocates yeast cell membranes localizing to an intracellular organelle. Our findings provide insights to the mechanism of Trp/Arg-rich antimicrobial peptides and rational for drug design criteria.

ID12 Tick-mediated Borrelia burgdorferi Infection of Nonhuman Primates for Assessment of Antibiotic Efficacy
M. Embers, Ph.D.
Research Assistant Professor, Tulane National Primate Research Center, Tulane University
members@tulane.edu

M. Embers, Ph.D., Nicole R. Hasenkampf, Lara A. Doyle-Meyers, Amanda C. Tardo and Mary B. Jacobs

Introduction: With over 30,000 new cases reported annually, Lyme disease is the most common tick-borne infection in North America. The causative agent, Borrelia burgdorferi, can chronically infect humans, causing rash, arthritis, carditis, and neurological dysfunction. A proportion of Lyme disease patients experience symptoms after antibiotic treatment and the etiology of those symptoms are a matter of debate. Our prior results have demonstrated that B. burgdorferi spirochetes, administered by injection, could persist in nonhuman primates (NHP) after antibiotic therapy. We aimed to test this again following tick-mediated infection. Methods: Ten macaques were tick-inoculated with B. burgdorferi and five were treated 4 months later with a 28-day course of doxycycline. Assessment for infection includes serology and xenodiagnosis. Results: All animals developed mild erythema at the sites of the tick bites, but only one developed a bona fide erythema migrans lesion. Months later, ticks fed upon monkeys for xenodiagnosis was efficient, but generated local papular lesions, indicating a moderate level of anti-tick immunity. We have begun the assessment of xenodiagnostic ticks for infection and the comprehensive serological analysis. Conclusions: Nonhuman primates exhibit variable local responses to tick-feeding and divergent antibody responses following infection with the identical strain of B. burgdorferi. A better understanding of diverse responses in an outbred population may help to improve the diagnosis of Lyme disease.
ID13  
A New Center of Biomedical Research Excellence on Pathogen-Host Interactions at Mississippi State University

Mark Lawrence, D.V.M., Ph.D  
Professor, Mississippi State University  
pruett@cvm.msstate.edu

Mark Lawrence, Stephen Pruett, Giselle Thibodeau Mississippi State University

A new COBRE is scheduled to begin at Mississippi State University in Fall 2013. The theme is pathogen host interactions. The projects cover a diverse set of pathogens, but a common component is the use of a systems biology approach and investigation of molecular mechanisms with the goal of developing a global understanding of pathogen and host responses to infection. Project 1 will examine the role of deubiquitinases (DUBS) and changes in expression of these enzymes in bacteria and in the host in response to infection with gastrointestinal pathogens including Shigella and Yersinia. Project 2 will focus on the mechanisms by which Listeria monocytogenes can resist bile salts, which are lethal to most bacteria. Project 3 will address the role of polyamine transport in the carrier state and in the pathogenicity of Streptococcus pneumoniae. Project 4 will address the mechanisms by which low concentrations of Staphylococcus aureus enterotoxins can suppress immunity and contribute to pathogenicity. Project 5 addresses the mutations of influenza viruses that determine changes in host specificity and organ tropism. The Investigators for these projects are: Mariola Edlelmann, Janet Donaldson, Bindu Nanduri, Keun Seok Seo, and Xiaofeng Wan. The Cores include the Institute for Genomics, Biocomputing, and Biotechnology (an existing facility with a full complement of equipment for proteomics, transcriptomics, and genomics), and the Cellular Purification and Analysis Core (Director, Giselle Thibodeau), which includes flow cytometry and cell sorting, confocal and electron microscopy, multiplexed bead array, and luminescence imaging (IVIS). These technologies have not previously been operated as a unified entity, as they will be for this COBRE. The Administrative Core will be directed by Mark Lawrence, leaving time for the P.I. (Stephen Pruett) to focus on mentoring and scientific activities. This work is supported by a COBRE grant from NIGMS (1P20GM103646).

ID14  
9-cis-Retinoic Acid and Troglitazone Impact Cellular Adhesion, Proliferation, and Integrin Expression in K562 Cells

Melissa D. Kelley, Ph.D.  
Associate Professor, University of Central Arkansas  
mkelley@uca.edu

Melissa D Kelley, Amanda M. Hanson University of Arizona

Retinoids have been established as pleiotropic regulators of both adaptive and innate immune responses. More recently, troglitazone, a PPAR gamma agonist, has been demonstrated to have anti-inflammatory effects. Although both retinoids and troglitazone are implicated in immune related processes, their combinatory role in cellular adhesion and proliferation has not been well established. In this study, the effect of 9-cis-retinoic acid (9-cis-RA) and troglitazone on K562 cellular adhesion and proliferation was investigated. Troglitazone exposure decreased cellular adhesion to RGD containing extracellular matrix proteins fibronectin, FN-120, and vitronectin in a concentration and time-dependent manner. In the presence of troglitazone, 9-cis-retinoic acid restores cellular adhesion to levels comparable to vehicle treatment alone on FN-120 and vitronectin substrates. Our study further demonstrates that troglitazone augments retinoid availability in K562 cells. Due to the prominent role of integrins in attachment to extracellular matrix proteins, we evaluated the level of integrin α5 subunit expression. Troglitazone treatment results in decrease in α5 subunit expression. Interestingly, in the presence of both troglitazone and 9-cis-RA, α5 subunit expression is restored to vehicle treatment alone. Further, using function-blocking antibodies, we demonstrate that both troglitazone and the combined treatment with 9-cis-RA prompts α5 integrin dependent cellular adhesion to FN-120. Finally, we show that the combinatory treatment of troglitazone and 9-cis-retinoic acid significantly damps cellular proliferation in K562 cells. Our study is the first to demonstrate that the amalgamation of troglitazone and 9-cis-retinoic acid influences cellular adhesion, retinoid availability, alters integrin expression, and damps cellular proliferation.
Construction and evaluation of a recombinant varicella vaccine expressing dengue virus antigens

Wayne Gray, Ph.D.
Professor, University of Arkansas for Medical Sciences
graywaynel@uams.edu

Wayne Gray, Jianzhong Cao, Univ. of Arkansas for Medical Sciences

Dengue virus (DV) causes a febrile, mosquito-transmitted, disease which causes over 100 million cases annually, especially in children and the elderly in tropical regions. Recent outbreaks in Florida, Texas, and Hawaii caution that dengue could become an emerging threat in the U.S. DV includes four distinct serotypes. While infection with one serotype induces immunity against that serotype, exposure to another serotype may cause dengue hemorrhagic fever or dengue shock syndrome. Live, attenuated varicella-zoster virus (VZV) vaccines offer protection against childhood varicella and herpes zoster in adults. VZV vaccines are candidates as recombinant vaccines expressing foreign antigens of other pathogens, including DV. The goal of this study is to construct a recombinant varicella vaccine expressing the antigenic DV envelope domain III (DVEDIII) of each DV serotype and to evaluate the ability of the vaccine to induce immune responses to DV in immunized animals. A chimeric gene expressing the DV EDIII epitope from each of the four DV serotypes was synthesized. The DVEDIII gene was inserted within ORF14 (gC) of the simian varicella virus (SVV) genome using the SVV cosmid genetic recombination system. Expression of the DVEDIII protein in rSVV-EDIII infected Vero cells was confirmed by immunofluorescence assay. Expression of the DV 1, 2, 3, and 4 EDIII antigens in rSVV-EDIII infected Vero cells was confirmed by immunofluorescence assay. The rSVV-DVEDIII virus replicated as efficiently as wild-type SVV in cell culture. The ability of the SVV-DVEDIII vaccine to induce neutralizing antibodies and cellular immune responses against DV serotypes 1-4 in immunized guinea pigs will be evaluated. A subsequent study will evaluate protection against DV challenge in immunized rhesus monkeys. This study provides a foundation for development of a recombinant VZV-DV vaccine to prevent DV disease in susceptible children and older adults.

Activation of the Innate Immunity by Respiratory Paramyxovirus infection

Ma. del Rocio Banos-Lara, Ph.D.
Post Doctoral Fellow, LSU
mdrbanos@lsu.edu

Ma. del Rocio Banos-Lara, Lindsey Harvey, and Antonieta Guerrero-Plata. Department of Pathobiological Sciences, Louisiana State University, Baton Rouge, LA

Respiratory syncytial virus (RSV) is a single stranded RNA virus belonging to the Paramyxoviridae family. RSV is the most important causative pathogen of respiratory illness in young children. RSV causes bronchiolitis, pneumonia, and has been associated with exacerbation of asthma. Currently, there has not been developed an effective vaccine against RSV. The first line of defense against pathogens including viruses is the innate immune response. This response is triggered by the recognizing of conserved structures called of pathogen-associated molecular patterns (PAMPs) by pattern recognition receptors (PRRs) on the host invaded cells. PRRs, including Nod-like receptors (NLRs) seem to play a critical role in the antiviral immunity. However, the role of NLRs in paramyxovirus infections is largely unknown. NLR family members like NLRP1, NLRP3, and NLRC4 form inflammasomes. Those structures activate the inflammatory cytokines IL-1 and IL-8, which ultimately activate to NF-KB. Some other members like NOD1 and NOD2 activate IRF-3, IRF-7 and NF-KB through RIP2, leading to the upregulating pro-IL-1, pro-IL-18, IL-6, TNF-alpha and type I interferon (IFN). On the other hand, NLRX1 and NLRCS, have been described as inhibitors of NF-KB signaling as well as inhibitors of Type I Interferon (IFN) production. In this work, we sought to determine the expression of NLRs induced by a Paramyxovirus infection in human epithelial cells. Our results show that RSV induced a differential expression of several members of the NLR family. The role of the different NLRs in RSV infection is warranted. Understanding the molecular mechanisms of activation of the innate immune response to RSV infection is critical to design new treatments and vaccine strategies to counteract the effects of this highly relevant respiratory viral disease.
**ID17**  
**Targeting Host Metabolic Pathways for Therapeutic Resolution of Virus- and Inflammation-Mediated Ocular Diseases**

Timothy P. Foster, Ph.D.  
Associate Professor, LSU Health Sciences Center, School of Medicine  
tfoste@lsuhsc.edu

Timothy P. Foster, James M. Hill, Christian Clement, Maria Sanchez, Paulo Rodriguez, and Augusto Ochoa.

Globally, infection- and inflammation-associated eye diseases are the leading causes of corneal blindness and visual morbidity, with over 500 million individuals affected. Pathogen-associated ocular diseases are a complex combination of pathogen-mediated trauma and host-mediated pathologies, often with the most severe sequelae being a consequence of host inflammatory responses. The leading infectious cause of corneal blindness in developed countries, Herpes Simplex virus type I (HSV-1), is present in 70-90% of the population and often affects the eye during episodes of reactivation. Despite effective antivirals against HSV, approximately 25% of the 450,000 Americans that have experienced ocular herpetic infections develop serious vision-threatening inflammation-associated stromal keratitis that can result in scarification of the cornea and an eventual need for corneal transplantation. We have developed an ophthalmic formulation (xTPF) that targets host-associated metabolic pathways that are required for replication of all viral pathogens, as well as induction of host inflammatory responses. Our studies have demonstrated in vitro and in vivo that xTPF: 1) is a safe, well-tolerated ophthalmic formulation; 2) promoted healing of pathogen- or surgically-induced wounds of the corneal epithelium; 3) inhibited the replication of all major vision-threatening ocular pathogens, including HSV-1 and HSV-2, VZV, CMV, Adenovirus, and Chlamydia. 4) prevented inflammation-associated disease sequelae in surgical and virus-infection ocular models. 5) possessed anti-neovascularization activities that prevented corneal vascularization and edema-associated corneal clouding. No current ophthalmic drug has all of these therapeutic properties. This data collectively suggests that by taking the novel approach of targeting host metabolic pathways, rather than pathogen replication mechanisms, therapeutic drugs can be developed with wide-ranging broadly applicable clinical potential.

**ID18**  
**Molecular and phenotypic characterization of Methicillin resistant S. aureus isolates from a hospital in South Mississippi**

Justin Batte  
Graduate Student, The University of Southern Mississippi  
justin.batte@eagles.usm.edu

Justin Batte, Dhiritman Samanta, Luis Marcos, Mohamed O. Elasri

Staphylococcus aureus remains the predominant reason of bacteremia around the world. The situation is worsened by the acquisition of antibiotic resistance. The health hazard burden caused by this species is severely exacerbated by worldwide dissemination of clones resistant to beta-lactam antibiotics (Methicillin Resistant Staphylococcus aureus; MRSA) in hospitals and communities. Methicillin resistance is conferred by a mecA gene located on a large chromosomal element SCCmec. The distribution of MRSA clones is dynamic and tends to be geographically unique. To understand the epidemiology of MRSA infections in a major hospital in South Mississippi, we performed a surveillance study with molecular typing and phenotypic analysis to determine the association of prevalent clones with their antimicrobial resistance profiles. A total of 137 MRSA isolates have been collected so far (period of May through July 2013). The isolates were subjected to antibioticogram analysis and Staphylococcal cassette chromosome mec typing by multiplex PCR. Among the isolates collected, 97 % were mecA positive, 28 % of these isolates were SCCmec type II and 69.7 % were SCCmec type IVa. Only 2 isolates were identified as type IVc and 1 isolate was type IVd. Antibiotic resistance profile revealed that 97 % of the isolates were resistant to oxacillin, 95 % resistant to erythromycin and all of them were resistant to augmentin (amoxicillin and potassium clavulanate). A significant number of isolates were also resistant to clindamycin (42 %) and linezolid (40 %). Only 4 isolates were resistant to Bactrim (trimethoprim and sulfamethoxazole). None of the isolates showed vancomycin resistance. In conclusion we identified both hospital (type II) and community (type IV) acquired isolates. This study will provide rationale for selecting antibiotics for treating patients with MRSA infection in this area.
ID19 Differential expression of histone H2B in yeast and mold morphotypes of a dimorphic pathogenic fungus Histoplasma capsulatum

Lacey Howard
Graduate Student, University of Southern Mississippi
laceyrlhoward@yahoo.com

Lacey Howard, Glen Shearer, University of Southern Mississippi

Histoplasmosis, a relatively common pulmonary infection, is caused by the dimorphic fungus Histoplasma capsulatum (Hc), which can be found in the mold (M) form in soils (or when grown in the laboratory at 25°C) or in the pathogenic yeast (Y) form in infected mammals (or when grown in the laboratory at 37°C). Histoplasma capsulatum is prevalent in soils fertilized by bird excrement in the Ohio/Mississippi River Valley region. Since the mold-to-yeast conversion is essential for pathogenesis, controlling the morphogenesis of this dimorphic fungus may be essential to controlling histoplasmosis. Elucidation of this differentiation/de-differentiation process may also yield information regarding reversible differentiation in other eukaryotes.

Our lab has identified a number of genes upregulated in the mold and yeast morphotypes. One such gene identified as strongly upregulated in the yeast morphotype was Histone H2B. H2B is involved in DNA packaging and thus may play a role in M-to-Y phase transition by allowing access to certain M phase genes while sequestering Y phase genes and vice versa. To analyze copy number and differential expression of HcH2B, Southern and northern blot were probed with HcH2B DNA from the G186AS strain. Real-time PCR was used to compare the differential expression from the northern blot. Southern blot analysis indicated that HcH2B appears to be a single copy gene. Northern blot analysis showed that HcH2B was more highly upregulated in the yeast phase. Currently we are attempting to construct H2B allelic replacement mutants to study the impact of loss of function of this gene. This work was supported by the Mississippi INBRE, funded by an Institutional Development Award (IDeA) from the National Institute of General Medical Sciences of the National Institutes of Health (P20GM103476) and National Science Foundation GK-12 Program to the University of Southern Mississippi, “Connections in the Classroom: Molecules to Muscles” (0947944).

ID20 Immunological effect of imiquimod and resiquimod in a DNA vaccination protocol with pA27L against smallpox

Osmarie Martínez-Guzmán
Graduate Student, University of Puerto Rico at Medical Science Campus
osmarie.martinez@upr.edu


In the event of a bioterror attack, the use of the current live-attenuated smallpox vaccine will be devastating for more than the 10 million immune-compromised individuals. We hypothesize that the adjuvant effect of toll-like receptors agonists will enhance the immune response of a DNA vaccine coding for Vaccinia A27L antigen, producing a protective immune response against vaccinia virus in a mice model. We tested our hypothesis analyzing the cellular-immune response by measuring the antigen specific lymphocyte proliferation by XTT proliferation assay and by identifying the IFN-γ production of splenocytes by ELISPOT. Also, we analysed the humoral-immune responses measuring total IgG and IgG2a/IgG1 ratios by ELISA, and the TH1 and TH2 cytokine profiles by protein microarray. Our ELISPOT data show means of 12, 378, 492, and 665 IFN-γ spot-forming cells corresponding to naive, A27L DNA, A27L DNA + Imiquimod, and A27L DNA + Resiquimod, respectively. Mice immunized with A27L plus adjuvants showed an increase in total IgG titer, compared to the non-adjuvanted groups. Moreover, mice immunized with A27L plus Imiquimod showed a higher IgG2a/IgG1 ratios as compared to animals immunized with antigen alone. Cytokine analysis shows that both IL-12 and IFN-γ increased after the vaccination with A27L plus Imiquimod, as compared to non-adjuvanted groups. Antigen specific lymphocytes proliferation was also observed in vaccinated groups as compared to naive. We conclude that the proposed vaccination cocktail is augmenting the A27L vaccine-mediated production of IFN-γ on mouse spleens, and an increase of the humoral immune response was observed with a TH1-biased response. Our vaccine is inducing a TH1 cytokine milieu, amplifying the antigen-specific activation of cytotoxic-T lymphocytes, important in viral infections. These results support our development of an effective adjuvant-mediated enhancement of the TH1 immune response in a vaccinia virus-free DNA vaccination platform.
ID21 Impact of vaccinia virus L3L gene in the immune response against smallpox, using a DNA-vaccination approach on a mouse model

Maite Ramirez
Graduate Student, University of Puerto Rico Medical Sciences Campus
mayte.ramirez@upr.edu


An intensive vaccination campaign using the current live attenuated vaccine against smallpox in the event of a bioterrorist attack will have catastrophic effects on a broad amount of the population, because of the known side effects caused by this vaccine, mostly in immune compromised individuals. Therefore, it is crucial to develop a safe vaccine that could be administered to a broad sector of the population. The L3L gene encodes for a virion protein required for the transcription of the vaccinia virus genes. We hypothesize that administration of L3L, as a DNA vaccine will induce a protective antigen-specific immune response. To validate our hypothesis we analyzed the cell- and humoral-mediated immune responses by ELISPOT and ELISA assays, respectively. Also, the cytokine profile was studied by protein microarray analysis. Our ELISPOT data show means of 53 and 421 IFN-γ spot-forming splenocytes corresponding to naïve and L3L DNA immunized mice, respectively. The TH1 and TH2 cytokine profiles established by protein microarray showed a production of 600 pg/mL of IFN-γ compared to undetectable levels found on naïve mice. Low IL-4 levels were observed in all groups. Antigen-specific lymphocyte proliferation was also observed in L3L-immunized mice as compared to naïve mice. Our L3L DNA vaccine formulation induces a TH1 cytokine milieu, that promotes antigen-specific activation of cytotoxic T-lymphocytes and lymphocyte proliferation, which are crucial in the generation of a protective immune response against viral infections. These results show an effective immune response in a vaccinia virus-specific DNA vaccination platform, using a novel gene whose immune response has not been fully characterized, to the best of our knowledge. We expect our approach to support the development of a vaccinia virus-free DNA vaccine. These data will be correlated with the qPCR analysis, developed in our laboratory, for viral load analysis in vaccinia-infected challenged mice.

ID22 Induction of Lin-Sca1+c-kit- lymphoid progenitor cells in the spleen during acute infection with Plasmodium yoelii

Debopam Ghosh
Graduate Student, University of Arkansas for Medical Sciences
DGHOSH@uams.edu

Debopam Ghosh, Brian D. Kennedy (UAMS) Jason S. Stumhofer (UAMS)

Hematopoietic stem and progenitor cells (HSPCs), characterized by the absence of lineage markers (Lin-) on their surface, are multi-potent cells that can give rise to different hematopoietic cell lineages. Although HSPCs are believed to replenish the immune system as a homeostatic reaction during infection and stress conditions, recent evidence implies they may directly perceive the presence of pathogens and become activated during infection. While bone marrow serves as the primary niche for hematopoiesis, extramedullary mobilization and differentiation of progenitor cell populations in the spleen occurs after Plasmodium infection. Here we identified a population of atypical HSPCs with a Lin-Sca-1+c-kit- (LSK-) phenotype in the spleen of C57BL/6 mice after infection with non-lethal Plasmodium yoelii 17X. This LSK- cell population was found to expand during infection (peaking at day 7 post-infection), and a proportion of the cells were found to produce the pro-inflammatory cytokine IL-17, but not IFN-γ. When transferred into naïve congenic mice, infection derived LSK- cells developed into mature B cells, and a population of IFN-γ–producing CD11c+NK1.1int cells that resemble a population of dendritic cells known as killer dendritic cells, indicating that LSK- cells may develop as an infection-induced progenitor cell population. In support of this idea in vitro coculture assays with OP9 stromal cells indicated that in the presence of parasitized RBC lysate the splenic LSK- cells proliferated and differentiated into B cells (CD19+B220+) much more vigorously than in the presence of growth factors that support lymphoid differentiation. This data suggests that these progenitor cells may sense the presence of parasite-derived pathogen-associated molecular patterns (PAMPs) directly, and become activated to generate effector immune cells to combat the infection and replenish the hematopoietic cell pool.
**ID23**  
**Study of the Role of the mold-specific MS95 gene in DNA Repair in the Pathogenic, Dimorphic Fungus**  
**Histoplasma capsulatum**

Erin Smith  
Undergraduate Student, The University of Southern Mississippi  
e.michelle.smith@eagles.usm.edu

Erin Smith, Logan Blancett, Dr. Davida Crossley, Dr. Glenmore Shearer, The University of Southern Mississippi  

Histoplasma capsulatum (Hc) is a dimorphic fungus that is the etiologic agent of the respiratory infection Histoplasmosis. In the environment, Hc exists as a multicellular, differentiated mold. The organism undergoes a shift to a unicellular, undifferentiated yeast once inhaled into the host’s lungs. This transition from mold to yeast is essential in the pathogenicity of Hc. Genes have been identified that are specific to the mold or yeast phase in an attempt to understand the molecular biology of this dimorphic shift. In our lab, MS95 was identified in a subtractive cDNA library that was enriched for genes upregulated in the mold morphotype. The gene was characterized via northern and southern blot analysis of four Hc strains, confirming that it is a mold-specific gene. Using NCBI genbank and BLAST analysis, it was found that MS95 is homologous to the DNA damage-responsive gene DDR48, which functions in DNA repair in Saccharomyces cerevisiae. Because of the homology, it is hypothesized that MS95 may be involved in DNA repair in Hc. In order to elucidate the function of MS95, a loss of function mutant was created via allelic replacement. In order to determine if MS95 is involved in DNA repair, wild-type as well as MS95 knockout mutant strains were grown on Histoplasma macrophage media (HMM) supplemented with varying concentrations of 4-nitroquinoline 1-oxide (4-NQO) or paraquat dichloride. These chemicals are known to cause oxidative stress, inducing DNA damage. Growth of both strains was monitored for any observable changes between the two strains indicating that MS95 plays a role in DNA repair. Future experiments include creating a complement of MS95 and over-expressing it in the yeast phase to further determine its role in Hc. This work was supported by Mississippi INBRE, funded by an Institutional Development Award (iDeA) from the National Institute of General Medical Sciences of the National Institutes of Health under grant number P20GM103476.

**ID24**  
**Understanding the mucus production of a human respiratory paramyxovirus infection**

Boyang Piao  
Undergraduate Student, Louisiana State University  
bpiao1@tigers.lsu.edu

Boyang Piao, MR. Banos-Lara. Louisiana State University M.Antonieta Guerrero-Plata. Louisiana State University

As one of the most clinically relevant respiratory virus in the hospitalization of young children, elderly, and immunocompromized patients, human metapneumovirus (hMPV) is a negative, single strand RNA virus that contains 9 proteins including three surface proteins: glycoprotein (G), fusion protein (F), and small hydrophobic protein (SH). The G protein is responsible for the virus attachment to cell receptors of the host cell, and it has been deemed as a potential vaccine candidate. hMPV mainly infects the upper and lower respiratory tract, replicating primarily in lung epithelial cells. Lung epithelial cells produce mucus which is consisted of mucins. Muc1, Muc 5ac and Muc 5b make up more than 90% of the mucus. However, little is known about their induction in response to hMPV infection. The primary objective of this work is to characterize the production of mucins during hMPV infection in vitro and in vivo and define the role of surface proteins in the production of mucus and mucins. Our results in vitro show that all three mucins have shown an increased expression at the protein and mRNA level, and that is directly proportional to the multiplicity of infection (MOI) and time of infection used. We have also observed that the production of mucins during an hMPV infection is dependent on viral replication. These critical findings have opened up the possibility of determining the role of Muc 1, Muc 5ac, and Muc 5b in hMPV infection in vivo by studying the mechanism(s) that regulate the production of mucins. Understanding the mechanisms of induction of mucins will be a relevant contribution in the design of a potential vaccine candidate for hMPV infection.
RNA-binding protein HuR plays a role in Th17 cells for induction of experimental autoimmune encephalomyelitis

Jing Chen, Ph.D.
Post Doctoral Fellow, Arkansas Biosciences Institute, Arkansas State University
jchen@astate.edu

J. Chen1,2,3*, J. Cascio4, J.D. Magee2, P. Techasintana2,4, R. Calaluce2, S. Yu3, U. Atasoy2,4,5 1Department of Veterinary Pathobiology, University of Missouri. 2Department of Surgery, University of Missouri. 3Arkansas Biosciences Institute, ASU

Effector functions of interleukin 17 (IL-17)-producing helper T cells (Th17 cells) have been broadly linked to the pathogenesis of multiple autoimmune diseases such as experimental autoimmune encephalomyelitis (EAE), a mouse model of multiple sclerosis (MS). Although the transcriptional regulation of Th17 cells is well understood, the posttranscriptional regulation of IL-17 gene expression, the signature cytokine of Th17 cells, remains unknown. Human antigen R (HuR), a member of the Hu family of RNA binding proteins, functions to stabilize many target mRNAs, such as IL-4, IL-13 and TNF-α, via binding the adenylate-uridylate-rich elements (AREs) present in the 3’ untranslated region (UTR). However, the regulation of IL-17 expression by HuR has not been established.

Recently we reported that production of IL-17 mRNA and protein, produced by polarized Th17 cells from HuR conditional knockout (KO) mice (OX40CreHuRf/f), are reduced. Moreover, using RNA immunoprecipitation and biotin pull down assays, we demonstrated that HuR directly binds to the 3’ UTR of IL-17 mRNA and prolong its half life. Mice with adoptively transferred HuR-/- Th17 cells had delayed initiation and reduced disease severity in the onset of EAE compared to wild type Th17 cells. Our results reveal a HuR induced posttranscriptional regulatory mechanism of Th17 differentiation which influences IL-17 expression. These findings may provide novel therapeutic targets for the treatment of Th17-mediated autoimmune neuroinflammation. *Current position: postdoctoral researcher with Dr. Carole Cramer, Dept. of Biology and Arkansas Biosciences Institute at ASU.

Time-course of effects of growth hormone (GH) and GH antagonist on auditory hair cell regeneration in zebrafish (Danio rerio)

Amy Ni
Undergraduate Student, Western Kentucky University
michael.smith1@wku.edu

Amy Ni, Mackenzie Perkins, Michael E. Smith Department of Biology, Western Kentucky University, Bowling Green, KY 42101

A previous microarray study found that growth hormone (GH) was significantly upregulated in the zebrafish (Danio rerio) inner ear following sound exposure (Schuck et al. 2011). In subsequent experiments, groups of zebrafish were exposed to a 150 Hz tone at 179 dB re 1 µPa RMS for 36 hours and then given an intraperitoneal injection of either carp GH or buffer. These studies showed that intraperitoneal injection of GH into zebrafish post-acoustic trauma, led to an increase in cell proliferation (BrdU-labeled cells), a decrease in cell death (TUNEL-labeled cells), and increased hair cell density compared to buffer-injected controls (Sun et al. 2011). The purpose of this study was to examine whether the effects of endogenous GH can be blocked with a GH antagonist, and whether exogenous GH injection prior to sound exposure has a prophylactic effect that may mitigate the effects of acoustic trauma on auditory hair cells. Groups of zebrafish were injected with either GH, GH antagonist, or buffer. Immediately following the injection, auditory hair cell damage was induced through exposure to acoustic overstimulation (150 Hz at 179 dB re 1 µPa). Hearing tests were performed on the fish at 0 – 5 days post-trauma via auditory evoked potential (AEP) recordings. Following AEP, fish ears were dissected and fixed overnight in 4% paraformaldehyde. Dissected zebrafish saccules were then subjected to fluorescein-conjugated phalloidin staining and visualized under florescence microscopy. GH injection pre-sound exposure improved hair cell density and promoted functional recovery of hearing, with GH-injected fishes exhibiting greater hair cell densities and lower hearing thresholds than buffer-injected controls. While GH has a positive effect on hair cell regeneration and hearing recovery, our results show that GH antagonist has the opposite effect. Whether GH is effective at preventing hair cell loss or promoting hair cell regeneration in mammals is yet to be determined.
Axon degeneration do shows apoptotic signatures

Yao Xu
Undergraduate Student, University of Central Arkansas
yxu1@cub.uca.edu

Yao Xu, Bhupinder Vohra

Axon degeneration is a pathologic hallmark of many neurological conditions, but the molecular mechanisms are still unknown. Since degenerating axons exhibit morphological features of apoptosis, we tested whether early or late apoptotic events are activated during the process of axon degeneration. We discovered that early apoptotic processes in the form of phosphatidylserine translocation takes place in axon degeneration. Even though the axonal degeneration is not blocked by caspase inhibition, we tested whether TLCK (an inhibitor of Trypsin like proteases which can also block cysteine proteases) can prevent axon degeneration. We found that TLCK blocked axon degeneration after trophic factor withdrawal by inhibiting activation of Caspase-6 in the axons. NGF deprivation activates glycogen synthase kinase 3 (GSK3) at the axon tip, which initiates an apoptotic signal that travels back to the soma to induce Jun-mediated neuronal apoptosis. We discovered that GSK3 inhibition protected the axons by inhibiting phosphatidylserine translocation and blocking caspase 6 activation in the NGF deprived axons. Intriguingly, although caspases are not involved in axon degeneration, which is caused by axotomy or vincristine, TLCK and GSK3 inhibition also inhibited axon degeneration in these conditions. Therefore, we believe that there are other caspase like proteases which are inhibited by TLCK and GSK3 might be playing a role in axon degeneration caused by axotomy or vincristine. Thus, we concluded that axon degeneration shares not only morphological features, but also distinct early and late activation pathways with apoptosis as well.

Cannabinoid receptor 1 models for protein structure based drug design of antagonists

Robert J. Doerksen, Ph.D.
Associate Professor, University of Mississippi
rjd@olemiss.edu


The cannabinoid 1 (CB1) receptor is expressed at high levels in the brain. CB1 antagonists and inverse agonists have potential to be used clinically to treat obesity, but there are currently no such drugs clinically available since the withdrawal of rimonabant from European markets due to adverse psychotropic indications in some patients. A hindrance to protein structure based drug design of neutral antagonists of CB1, which may have reduced negative psychotropic effects, is that so far no experimental crystal structure of the cannabinoid 1 (CB1) receptor is available. To better understand antagonist binding to the CB1 receptor and to provide 3D homology models for virtual screening, we prepared several sets of protein models of the CB1 receptor based on the several available G-protein coupled receptor X-ray crystal structures, using a variety of computational approaches and software. We selected the best models and validated them using enrichment of docking of known CB1 antagonists from amongst a large set of decoy compounds. We are using the validated CB1 models for docking of natural products isolated from psychoactive plants and for virtual screening of marine-derived natural products and synthetic compounds.

Acknowledgements: Grant no. P20GM104931 from the National Institute of General Medical Sciences (NIGMS), a component of the National Institutes of Health (NIH) and C06 RR-14503-01 from the NIH National Center for Research Resources (NCRR),
NS09  Uncovering the characteristic features of the active state 3D structure of the human cannabinoid subtype 2 receptor

Kuldeep K. Roy, Ph.D.
Post-Doctoral Research Associate, The University of Mississippi
kkroy@olemiss.edu

Kuldeep K. Roy, Ph.D., Pankaj Pandey and Robert J. Doerksen* Department of Medicinal Chemistry, School of Pharmacy, University of Mississippi, University, MS, USA 38677

The most significant breakthrough in crystallographic studies of G-protein coupled receptor (GPCR) active states has been the X-ray structure determination of the β2-adrenergic receptor-Gs complex. In addition, there are other X-ray structures of Class-A GPCRs available in their active states that can be used for homology modeling of the active states of the GPCRs using multi-template based protein structure prediction. Meanwhile, continuous improvement has been made in protein structure prediction methods for providing good-to-high quality models depending upon the local and global homology between target and template(s) sequences. These advances have opened new perspectives for structure-based drug discovery. The cannabinoid receptor subtype 2 (CB2) is a GPCR from the cannabinoid receptor family. The development of selective CB2 agonists (with minimal affinity for CB1) may provide clinical candidate drug(s) for neuropathic pain and inflammatory disorders. In the absence of any X-ray crystal structure, computational modeling and simulation of the active-state conformation of the human CB2 receptor may advance our understanding of the CB2 agonist binding and activation mechanism, and could be useful for the structure-based discovery of CB2 agonists. Here, through a systematic homology modeling and molecular dynamics simulations (MDS) protocol, we uncover the characteristic features of the active state 3D structure of the human CB2 receptor (Sequence ID: P34972), mode of agonist recognition, and agonist-induced conformational changes during receptor activation. The computational insights gained from the present study may further be used in the structure-based discovery of selective CB2 receptor agonists.

NS10  Fenofibrate extends survival in the SOD1G93A mouse model of amyotrophic lateral sclerosis

Shilpi Yadav, Ph.D.
Post-Doctoral Fellow, University of Arkansas for Medical Sciences
mkiaei@uams.edu

Shilpi Yadav, Ph.D., Shilpi Yadav, Rachel D. Hendrix, Mohammad A. Esmaeili, §Noel Y. Calingasan, §M. Flint Beal, and Mahmoud Kiaei. Department of Neurobiology and Developmental Sciences, Center for Translational Neuroscience, University of Arkansas for Medical Sciences, Little Rock, AR, USA-72205 § Department of Neurology and Neuroscience, Weill Medical College of Cornell University, New York, NY

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease without any cure. Fibrates such as Fenofibrate (FF) and Bezofibrate, in general are pan-PPAR agonists. FF has major impact on PPARα, and is a member of the fibrate class of hypolipidemic drugs, which has been extensively used to treat hypertriglyceridemia and mixed hyperlipidemia. It belongs to the broad class of chemicals known as peroxisome proliferators (PPs), which act through the peroxisome proliferator–activated receptor α (PPARα). We performed a pre-clinical study in the SOD1G93A mouse model of ALS in which FF was administered at 200 mg/kg/day and body weight, motor performance, survival were assessed. Our results show that the mice treated with FF had attenuated weight loss and enhanced motor performance, and increased survival as compared to vehicle treated SOD1G93A mice. Spinal motor neuron counts were significantly increased in the FF treated mice as determined using Nissl staining. Cytochrome c release from mitochondria in the spinal cord neurons was blocked. PGC1-α levels were increased in the spinal cord of the FF treated mice, as compared to untreated mice. These observations show that FF significantly increased the life span and reduced neuronal degeneration in a transgenic mouse model of ALS. Further study is needed to fully understand the neuroprotective mechanisms of action of FF in ALS. Since FF has excellent record of safety in patients with high cholesterol, this drug can be quickly moved to clinical studies in ALS. Acknowledgements: Authors acknowledge the support by grants from University of Arkansas for Medical Sciences startup fund, and University of Arkansas for Medical Sciences Center for Translational Neurosciences. Also, authors acknowledge the support by grants from the National Center for Research Resources (5P20RR020146-09) and the National Institute of General Medical Sciences (8 P20 GM103425-09).
Kevin Garrison, Ph.D.
Associate Professor, University of Central Arkansas
kgarrison@uca.edu

Kevin Garrison, Ph.D., Michelle Settle, M.S.,PT Chad Lairamore, PT, Ph.D. Mark Mennemeier, Ph.D.

Transcranial direct current stimulation (tDCS) is a method of non-invasive brain stimulation. tDCS delivers weak polarizing direct current to the cortex via electrodes placed on the scalp - an active electrode overlying the cortical target, and a reference electrode over the contralateral supraorbital area. tDCS over superficial neural structures (ie upper extremity motor cortex) induces sustained changes in the neural cell membrane potential: cathodal tDCS leads to brain hyperpolarization (inhibition), whereas anodal results in brain depolarization (excitation). However, investigating the effects of tDCS on cortical excitability of the lower-extremity motor cortex, has yet to be established. Cortical excitability is measured by establishing a recruitment curve derived from motor-evoked potentials (MEPs) recorded from the contralateral tibialis anterior (TA) muscle. MEPs are elicited by single-pulse transcranial magnetic stimulation (TMS) delivered at increasing intensity. Changes in the slope of the curve are indicators of changes in cortical excitability. While using a figure-8 TMS coil to obtain recruitment curves for the TA muscle in healthy subjects, we frequently exceeded stimulator output before the curve could become established. We overcame this by using a double-cone coil, and by having the subject isometrically contract the TA. We found that ipsilateral contraction enhances contralateral MEPs. We tested this method in healthy subjects before, immediately after, and 1 hour after receiving 10 minutes of anodal tDCS or sham tDCS. MEP maximums increased after anodal tDCS for up to 1 hour and recruitment curves became steeper, indicating a lower threshold (i.e., an increase in cortical excitability). Similar changes were not seen for sham tDCS. We hypothesize that anodal tDCS may also be used to make stroke patients more responsive to gait training by priming the cortex and increasing lower-extremity cortical excitability prior to administering therapy.

Abdallah Hayar, Ph.D.
Associate Professor, University of Arkansas for Medical Sciences
amhayar@uams.edu

Abdallah Hayar, Center for Translational Neuroscience, Dept. of Neurobiology and Developmental Sciences, Univ. of Arkansas for Medical Sciences, Kathryn A Hamilton, Dept. of cellular Biology and Anatomy, Louisiana State University

Olfactory bulb output neurons exhibit highly-synchronized activity in brain slices despite that they are deprived from their normal sensory input. The olfactory bulb is also rich in dendrodendritic synapses and gap junctions, both of which can facilitate the synchronization. In a previous study, we found that external plexiform layer (EPL) interneurons (INs) and tufted cells exhibit EPSC and spike bursting, respectively. EPL INs could therefore play an important role in integrating activity via their dendrodendritic interactions with surrounding output neurons. We have now obtained intracellular patch clamp recordings (HP = -60 mV) from single EPL INs and simultaneous extracellular recordings from 1- 3 output cells centered around the interneuron within a ~ 100 µm-wide column perpendicular to the glomerular layer. Auto- and cross-correlation analysis methods were used to determine if interneuron EPSCs were correlated with mitral/tufted (M/T) cell spikes. We have obtained positive correlation between the IN EPSCs and the spike bursts of T cells located in several different EPL sublaminae and also with mitral cells. These results indicate that some EPL INs receive inputs from several different M/T cell subtypes. Moreover, we found evidence for direct monosynaptic connections between some INs and M/T cells. This was demonstrated by the high probability of occurrence of an IN EPSC immediately following a spike in a paired output cell as shown by the presence of a sharp peak (width 1-2 ms, lag 1 ms) superimposed on a relatively broad peak of crosscorrelation (width ~ 500 ms). Our data suggest that EPL INs integrate information from different output cell types that might not be necessarily affiliated with the same glomeruli. The presence of relatively high level of neuronal interactions in the olfactory bulb circuit could be attributed in part to the fact that all olfactory bulb neurons must tune their activity to the respiratory cycle.
Heart Rate Variability and PTSD and the Effect of Over-reporting

Jeff Pyne, M.D.
Professor, Central Arkansas Veterans Healthcare System and University of Arkansas for Medical Sciences
jmpyne@uams.edu

Jeff Pyne, M.D., Robert Brady, Central Arkansas Veterans Healthcare System  Tim Kimbrell, Central Arkansas Veterans Healthcare System  Susan Jegley, Central Arkansas Veterans Healthcare System

Physiological assessment of post-traumatic stress disorder (PTSD) presents an additional avenue for evaluating the severity of PTSD symptoms. We investigated whether a symptom report style characterized by the endorsement of uncommon symptoms attenuated the relation between self-reported PTSD symptoms and heart rate variability (HRV). Participants were 115 returning Veterans from the OEF/OIF operations with or without PTSD. The Clinician Administered PTSD Scale (CAPS) was used to assess PTSD symptom severity. Symptom over-report was assessed using the Miller Forensic Assessment of Symptoms Test (M-FAST). Hierarchical linear regression was used to test the main effects of PTSD severity and over-reporting, and their interaction, after controlling for the well-established effect of age on HRV. Age was entered in the first step, followed by the main effects of CAPS and M-FAST entered together in a second step, and the interaction in a third step. The main effect of CAPS was significant ($\beta = -0.27, p < .05$), showing that HRV declined as a function of PTSD severity. The main effect of M-FAST was not significant ($\beta = -.05, p = .62$). Importantly, the interaction between CAPS and M-FAST was significant ($\beta = -.27, p < .05$). Post-hoc probing of the simple effects of the interaction revealed that PTSD was a significant negative predictor of HRV, but only at higher levels of over-reporting. These findings demonstrate that Veterans with PTSD who show a tendency for symptom over-report also exhibit baseline physiology similar to those without an over-reporting style, and may in fact exhibit worsening physiology as a function of PTSD severity. Moreover, the results indicate that the relation between PTSD severity and HRV is strongest among individuals with a symptom reporting style characterized as “over-reporting”. This may reflect the possibility that the relation between PTSD and HRV is partially determined by perceived distress that is not captured by PTSD symptoms.

The Relationship Between Modified Stroop Effect, PTSD Symptoms and Response Style in OEF/OIF Veterans

Tim Kimbrell, M.D.
Associate Professor, University of Arkansas for Medical Sciences; Center for Translational Neurosciences; Central Arkansas VA Healthcare System
timothy.kimbrell@va.gov

Tim Kimbrell, Joe Constans (SE Louisiana Veterans Healthcare System, Tulane University; Theresa Kramer (University of Arkansas for Medical Sciences) Susan Jegley (Central Arkansas VA Healthcare System; Jeff Pyne (Central Arkansas VA Healthcare System; University of Arkansas for Medical Sciences)

Introduction: Over reporting of symptoms has been hypothesized as an explanation for the lack of specificity in the use of behavioral measures in the study of posttraumatic stress disorder (PTSD). Individuals with PTSD are slower in naming the color of trauma-related words relative to trauma-irrelevant words compared with trauma-exposed controls. This Modified Stroop effect (MSe) is hypothesized to occur because individuals with PTSD involuntarily allocate attention to the threat content of the stimulus rather than the font color. We examined the interrelationships among PTSD, over-reporting response bias, and the MSe in Veterans of Operation Enduring Freedom and Operation Iraqi Freedom (OEF/OIF). Methods: 124 OEF/OIF Veterans completed the Clinician Administered PTSD Scale, PTSD checklist, Miller Forensic Assessment of Symptoms Test and a MST. The recorded verbal response latencies to neutral, social threat and combat related words served as the primary dependent variable. Participants were categorized into PTSD+/PTSD- and Over-reporting+/Over-reporting- groups. Results: A combat threat interference index calculated by subtracting neutral word color-naming latency from combat word color-naming latency was used as the dependent variable in a one-way ANOVA with Group as the single between-subject factor. Multiple comparisons between the groups using Tukey’s post hoc tests showed that differences between PTSD-/Over-reporting- and PTSD+/Over-reporting- approached significance (p = .079). Differences between PTSD+/Over-reporting+ and both PTSD+/Over-reporting- and PTSD-/Over-reporting- were significant (ps=.046 and .002, respectively). Conclusion: We found that the presence of an over-reporting response style was associated with an augmentation of the MSe in OEF-OIF Veterans with PTSD. The MST does not appear add any additional information to PTSD diagnostic validity beyond that conferred by a structured clinical interview.
rTMS restores functional connectivity of auditory cortex in schizophrenia with auditory hallucinations; a case study

Justin Powell, M.D.
Resident, University of Arkansas for Medical Sciences
GAJames@UAMS.edu

Justin Powell, Shanti Prakash Tripathi, M.S. - University of Arkansas for Medical Sciences
Mark Mennemeier, Ph.D. - University of Arkansas for Medical Sciences
Erick Messias, M.D., Ph.D. - University of Arkansas for Medical Sciences


Methods: We initiated a double blind, sham controlled, clinical trial comparing two locations (vertex and temporal cortex – BA22) and two frequency of stimulation (1 or 10 Hz). We report findings for one patient with schizophrenia and seven healthy control participants.

Results: Consistent with previous reports, the baseline connectivity of left and right Heschl’s gyrus was significantly lower for the patient with schizophrenia (r=0.04) than for healthy control participants (mean r=0.58; t(5)=22.1, p<0.0001). Connectivity of these two regions did not change with sham rTMS (r=0.04), increased with 1Hz and 10Hz rTMS (mean r=0.20), but diminished after a two month wash-out period (r=0.10). Discussion: This preliminary data suggest that rTMS can increase the functional connectivity of the primary auditory cortices to more closely resemble the connectivity observed in healthy subjects without schizophrenia. Future work will relate auditory cortex functional connectivity to therapeutic response to rTMS in a larger sample Support comes from the Center for Translational Neuroscience, University of Arkansas for Medical Sciences (P20 GM103425).

Continuous EEG Monitoring in the Neonatal Intensive Care Unit: Detection and Treatment of Clinical and Subclinical Seizures

Dorothy J. Currey
Graduate Student, University of Arkansas for Medical Sciences Center for Translational Neuroscience (COBRE)
mulkeysarah@uams.edu

Dorothy J. Currey University of Arkansas for Medical Sciences Center for Translational Neuroscience University of Arkansas, Fayetteville Honors College Arkansas Children’s Hospital Research Institute Vivien L Yap, M.D. University of Arkansas for Medical Sciences Department of Pediatrics

Background: Continuous electroencephalography (cEEG) monitoring is used in neonatal intensive care units (NICU) to detect seizures. The highest lifetime incidence of seizures is in the neonatal period; however neonatal seizures may be subclinical and not clinically evident due to electroclinical dissociation. Limited information is available concerning infant characteristics of those with clinical and subclinical seizures in the NICU. Objective: To identify and compare characteristics of infants with clinical and subclinical seizures undergoing cEEG monitoring. Methods: A single-center, retrospective chart review of all infants with at least one cEEG of ≥1hour duration performed in the Arkansas Children’s Hospital NICU from January 1, 2010 – June 30, 2013 was performed. Indication for monitoring, clinical characteristics, and cEEG interpretation was determined for each infant and compared between the clinical and subclinical seizure groups. Results: One hundred fifty seven infants with a mean gestational age of 36.2 weeks underwent cEEG monitoring. Of the 57 infants with electrographic seizures during the initial cEEG recording, 54% (n=31) had subclinical seizures with no clinical correlate on the accompanying video. There was no significant difference in patient characteristics between clinical or subclinical seizure groups. The most common indication for cEEG in both groups was an event suspected to represent seizure. Acute brain injury was the most common primary diagnosis in the clinical seizure group, while hypoxic-ischemic encephalopathy was most frequent in the subclinical group. An unfavorable outcome was seen in 65% (31/48) of infants with electrographic seizures. Conclusion: Seizures are common in high-risk NICU infants undergoing cEEG monitoring, with the majority of electrographic seizures not clinically apparent. cEEG monitoring of high-risk NICU patients, even those with clinical seizures, is therefore needed for accurate diagnosis and management.
Comparison of infarct volume and neurological functions at 6 and 24 hours in a rat model of stroke

J.A. Montgomery, M.D.
Resident, University of Arkansas for Medical Sciences
RDSkinner@uams.edu

*Montgomery, J.A. (1), Nix, J.S (1), Arthur, M.C. (1), Brown, A.T. (1), Lowery, J. (2), Brown, J.A. (1), Lowery, J.D. (1), Skinner, R.D. (3), Borrelli, M.J. (1) and Culp, W.C. (1) (1) Department of Radiology, University of Arkansas for Medical Sciences, Little Rock, AR (2) Department of Laboratory Animal Medicine, University of Arkansas for Medical Sciences, Little Rock, AR (3) Department of Neurobiology and Developmental Sciences and Center for Translational Neuroscience, University of Arkansas for Medical Sciences, Little Rock, AR * Presenting author

Introduction: The importance of accurate and reliable infarct volume and neurological assessment is unquestionable in stroke research. One useful procedure for inducing and studying stroke is surgical occlusion of the middle cerebral (MCA) and common carotid arteries (CCA). Since the size and effects of a focal stroke may increase over time, the current study assessed infarct volume and neurological performance at 6 and 24 hours following surgery. Hypothesis: Infarct volume and neurological assessment scores (NAS) will not significantly differ between 6 and 24 hours in a rat permanent occlusion model of stroke.

Methods: Spontaneously Hypertensive Rats were randomly assigned to 6 (n=11) and 24 (n=8) hour sacrifice groups. Rats underwent surgical cauterization of the MCA followed by ligation of the CCA. Immediately prior to euthanasia at 6 or 24 hours, rats received a neurological exam and an NAS value. Neurological assessment consisted of an 18 point scale for reflexes, balance and walking on a beam, and motor and sensory tests. Brains were harvested after sacrifice and treated with vital stain to demonstrate areas of infarct. Infarct volume was then quantified using NIH ImageJ software and reported as percentage of the total brain volume measured. Results: Mean percent infarct volumes ±SE measured at 6 and 24 hours were 8.75% ±1.87 and 12.12% ±2.81 respectively, yielding a P value of 0.31. The mean NAS score ±SE for the 6 hour group was 10.55 ±1.07 while the 24 hour group was 6.71 ±1.70, giving a value of P=0.06. Conclusion: Though there was no significant difference between 6 and 24 hour groups for either NAS or percent infarct, NAS scores trended higher for the 6 hour group. The larger NAS values at 6 hours may indicate more temporary deficits due to edema or the residual of anesthetic. Larger numbers of animals are required to assess this.
Dodecafluoropentane (DDFP) tissue distribution following multiple doses of emulsion in the New Zealand white rabbit

M.C. Arthur, Ph.D.
Research Assistant, University of Arkansas for Medical Sciences
RDSkinner@uams.edu


*Presenting author

Intravenous injection of Dodecafluoropentane emulsion (DDFPe) increases oxygen transportation and reduces infarct volume in the rabbit with effects lasting at least 90 min after injection. DDFP organ distribution is critical to understanding the mechanism and efficacy of the compound in treating ischemia. Previous studies indicated rapid DDFP elimination from the blood (t1/2 = 2 min). Disparity between blood concentration and effect means that traditional pharmacokinetics (PK) are not predictive. We describe DDFP tissue disposition under three different dosing regimens. DDFP concentrations were determined in the brain, heart, kidney, liver, spleen, and lung. Eleven New Zealand white rabbits had intravenous catheters in the right ear. Three treatment groups were administered 0.6ml/kg 2% DDFPe at 90 min intervals then sacrificed at designated times. A 1 dose group (N=3) was sacrificed 2 minutes following injection, and a 4 dose group (N=3) and 15 dose group (N=4) were sacrificed 90 min after the final injection. Tissues were harvested from each organ, divided into 1-2 g samples (N=3) followed by multiple injection headspace sampling/GC/MS determination of DDFP. [Headspace analyzer kindly provided by the Center for Translational Neuroscience.] DDFP quickly distributed to all tissues sampled with the highest concentration in the spleen. A significant and steady increase in concentration was observed in the brain and heart. Following 15 doses, DDFP concentrations were equally distributed between lung, liver, kidney, and spleen (250 µg/g). The relationship between DDFP lung concentration and dose number was complex suggesting that DDFP concentration in the lung is dependent on changes in respiration. The steady increase in DDFP brain concentration indicated that DDFP reaches the site of action (brain) at a therapeutic concentration after multiple doses. Future studies will optimize this dosing regimen to optimize therapeutic effects and minimize toxicity.
Dodecafluoropentane Emulsion Reduces Brain Infarct Volume and Neurological Deficit in a Sprague Dawley Rat Stroke Model

A.T. Brown, Ph.D.
Post Doctoral Fellow, University of Arkansas for Medical Sciences
RDSkinner@uams.edu


Dodecafluoropentane emulsion (DDFPe), a perfluorocarbon approved for human use in Europe as an ultrasonographic contrast agent, has been shown in a rabbit permanent occlusion model of stroke to deliver oxygen as a nanodroplet to tissues suffering from ischemia, resulting in a >80% reduction in infarct volume compared to controls. We investigated the tissue-saving action of DDFPe in a second animal ischemic stroke model of permanent occlusion using Sprague Dawley (SD) rats and the effect of DDFPe on neurological outcomes. Hypothesis: Intravenous DDFPe will reduce the brain % infarct volume (%IV) and neurological deficit compared to controls. Methods: SD rats (n=26) underwent cauterization of the middle cerebral artery followed by ligation of the common carotid artery. Controls (n=11) received no treatment while treatment groups received either 1 (n=7) or 4 (n=8) doses of 2% w/v DDFPe at 0.6 mL/kg. The 1 dose group was injected 1 hour post-occlusion while the 4 dose group was additionally injected every 90 minutes until euthanasia. Neurological exam was given before sacrifice at 6 hours post-occlusion. Brain tissue was treated with vital staining and %IV of total brain was measured. Results: The mean %IV for each group was 3.02 ± 0.74% (mean ± S.E.) for 1 dose, 1.70 ± 0.80% for 4 doses, and 8.76 ± 1.92% for controls. %IVs were significantly reduced compared with controls (P=0.01 for 1 dose and P=0.002 for 4 dose). The 1 and 4 dose groups did not differ significantly (P=0.57). Neurological scores were improved in the 4 dose treatments (5.75 ± 1.10) compared to controls (9.20 ± 1.17) at P=0.05. There was no significant difference between the 1 dose (8.43 ± 1.40) and control group (P=0.68). Conclusion: The current study demonstrates the ability of DDFPe to reduce infarct size and preserve neurological function. Considering the success of this and previous studies including prior safety profiles it is clear that DDFPe should be moved to clinical stroke trials.

The Animal Behavior Core (ABC) of the COBRE Center for Psychiatric Neuroscience (CPN)

Ian A. Paul, Ph.D.
Professor, University of Mississippi Medical Center
ipaul@umc.edu

Ian A. Paul, Ph.D., Leia Golden, University of Mississippi Medical Center

The final common pathway of all CNS activity is the behaving organism. Moreover, behavior is plastic, changing during development, in response to the environment and in response to disease states. Dissecting and analyzing behavior over an animal’s lifetime requires observation at levels ranging from simple component behaviors such as sensation to integrated behavioral processes like learning and memory. This range of observation requires customized facilities, equipment considerable technical expertise. The ABC was created by the CPN to serve the needs of researchers at UMMC and other facilities address these needs. Mission. The mission of the ABC is to improve the scope and competitiveness of functional CNS research at UMMC, COBRE and INBRE facilities in Mississippi by providing researchers with: 1) the tools and assistance to identify and monitor animal behavior across species; 2) training in state-of-the-art techniques in the analysis of behavior and; 3) assistance with the interpretation and presentation of data and results relating to behavior. Services. The ABC provides a centralized base of physical space, equipment, expertise and protocols for investigators seeking functional behavioral measures of CNS activity under normal and pathological conditions. It provides investigators with the means to phenotype animal behaviors under a variety of treatments and conditions. Support Provided. Investigators have the option to contract with the ABC to conduct specific procedures themselves using ABC facilities or utilize the support of ABC technical staff on a fee for service basis. The fee schedule is available at http://www.umc.edu/Research/Core_Facilities/Core_Facilities_Home.aspx. Supported by P30 GM103328 and the University of Mississippi Medical Center.
NS22  
D-amphetamine withdrawal paradigm in methamphetamine dependence

M.J. Mancino, M.D.
Assistant Professor, University of Arkansas for Medical Sciences (UAMS)
mjmancino@uams.edu

M.J. Mancino, M.D., J. McGaugh, University of Arkansas for Medical Sciences, J. Thostenson, University of Arkansas for Medical Sciences, D. K. Williams, University of Arkansas for Medical Sciences, A. Oliveto, University of Arkansas for Medical Sciences

Aims: Treatment-seeking methamphetamine (METH) dependent individuals were enrolled in a 4-wk, double-blind, placebo-controlled trial examining the impact of abruptly terminating oral d-amphetamine (DEX) in METH dependent humans on withdrawal, sleep, and cognition. Methods: Participants were admitted to a residential facility, inducted onto DEX during wk 1, randomized by severity of METH dependence, sex, METH Withdrawal Assessment (MAWA) score and ADHD history to receive DEX or placebo (PLA) during wks 2-3. Participants received PLA during wk 4. Participants received standard treatment for substance abuse. Assessments (vitals, mood, cognitive performance, withdrawal/craving scores, sleep measures) were completed at least weekly. Results: 14 METH-dependent volunteers (6 male, all Cauc, mean age 35.6 yrs) completed at least 2 wks of the study. Baseline characteristics did not differ between grps, except age (DEX=39.1±6.7, PLA=32.0±5.0; p=0.04). Preliminary analyses indicate “desire for METH” mean scores differed at the end of week 2 (DEX=1.0±1.7, PLA=10.7±10.7; t=-2.52, p=0.04) and a trend toward significant time (t=2.2, p=0.06) and grp time interaction (t=1.97, p=0.09). Though there were significant decreases in supine (t=2.88, p=0.02), seated (t=3.19, p=0.02) and standing (t=3.25, p=0.01) HR between wks 1 and 2 in the PLA grp, no significant changes in HR were found in the DEX grp. Conclusions: To our knowledge, this is the first double blind, PLA-controlled trial measuring pharmacologic effects of abruptly stopping amphetamine in METH dependent humans. Preliminary results suggest this amphetamine withdrawal paradigm may be useful in examining the efficacy of pharmacologic agents in alleviating early METH withdrawal symptoms.

NS23  
A Novel Model For Investigating And Reversing H-Reflex Changes In Chronic Spinal Cord Injury In Rat

Nancy B. Reese, Ph.D., P.T.
Professor, Center for Translational Neuroscience, University of Central Arkansas
nancyr@uca.edu

Nancy B. Reese, Ph.D., P.T. Arfaj A Center for Translational Neuroscience Skinner RD Center for Translational Neuroscience

Spinal cord injury (SCI) results in hyperreflexia over time. Previously, we demonstrated that separate groups of adult rats transected at T8 and tested at various time points transitioned to hyperreflexia beginning at 14 days post SCI (Yates, 2008), and this could be prevented by passive exercise of the hind limbs during cycling (MBET). However, the transition to hyperreflexia and its reversibility have not been well studied in a single group of SCI rats over time. Methods: Adult female SD rats (n=18) were studied: transection only (TX; n=6), transection+MBET (EX; n=6), and transection+L-dopa (LD; n=6). Frequency-dependent inhibition of the HR was measured at 0.2, 1, 5, and 10 Hz in each rat before surgery (controls) and on days 7, 14, 30, 45, 60, 75, and 90 following surgical transection of the spinal cord at T8. All testing was done in awake rats using surface electrodes. The TX group received no further treatment. The EX group underwent 60 days of MBET starting on day 30 post-SCI. The LD group received L-dopa daily starting on day 30 post-SCI for 60 days. Results: Repeated measures ANOVA revealed a significant interaction effect of group and frequency (p<0.01). When groups were combined, HR amplitude was significantly different 30 days post-SCI vs controls at 1 Hz (p<0.05) and 5 and 10 Hz (p<0.01). In the TX group, at 90 days post-SCI HR amplitudes were different from control and 30 day values at all frequencies (p<0.01). By 90 days post SCI HR values were different from their 30 day values at 5 Hz (p<0.05) for the LD group and at 10 Hz (p<0.01) for LD and EX groups (i.e., hyperreflexia was decreased). At 90 days, HR values in EX and LD groups were significantly lower than in the TX group at 5 and 10 Hz (p<0.01). Conclusions: This technique allowed measurement of H-reflexes pre and post SCI in the same animals longitudinally over time. Results revealed the potential of passive exercise and L-dopa to reverse the hyperreflexia caused by complete chronic SCI.
Multiple Sclerosis (MS) is a debilitating disease in which the immune system attacks myelin, a fatty substance that insulates nerve fibers, and disrupts normal signal conduction. Studying the development of the cells that produce myelin could lead to a better understanding of the systems affected by the disease and ways to combat its progression. The proteolipid protein (PLP) gene is known to be expressed in oligodendrocytes of the central nervous system (CNS), and its product is the main protein found in myelin. The PLP gene has also been found to be expressed in Schwann cells in the dorsal root ganglia (DRG) of the peripheral nervous system (PNS) (Puckett et al., J. Neurosci. Res. 18:511-518.). To examine the regulation of PLP gene expression, two transgenic mouse lines which express a lacZ reporter gene under the control of PLP promoter elements have been created. One line of mice was created using human PLP1 genomic sequences that include 6.2 kb of 5'-flanking DNA, the first exon and the first intron of the gene (777). The other transgenic line uses mouse genomic sequences that include 2.4 kb of 5'-flanking DNA, the first exon and the first intron of the PLP gene to drive lacZ expression (26H). Since the PLP-LacZ transgene has been found to be expressed in the 26H line at embryonic day (E) 14.5 in the DRG (Wight et al., J. Cell. Biol. 123:443–454) we hypothesize that it is expressed specifically in embryonic glial cells. To test this hypothesis, we performed double label immunohistochemistry, as well as, double label in situ hybridization at E10.5, E12.5, and E14.5 with markers of the reporter gene combined with markers of neural and glial cell-types. We found expression of the reporter gene in neurons in the 777 line indicating that it is not specifically expressed in glial cells. We are currently characterizing the expression of the reporter gene in the 26H line. Supported by the Summer Mentored Faculty Fellowship Program of the Arkansas INBRE (P20 RR 16460).
NS26  Exploring a Profile of Biomarkers for Preoperative Brain Injury in Newborns with Congenital Heart Disease

Sarah B. Mulkey, M.D.
Assistant Professor, University of Arkansas for Medical Sciences Center for Translational Neuroscience (COBRE)
mulkeysarah@uams.edu

Sarah B. Mulkey, M.D., Christopher J Swearingen, Ph.D. University of Arkansas for Medical Sciences Department of Pediatrics
Maria S Melguizo, M.S., University of Arkansas for Medical Sciences Department of Pediatrics
Xiawei Ou, Ph.D. University of Arkansas for Medical Sciences Department of Radiology
Adnan T Bhutta, MBBS University of Arkansas for Medical Sciences Department of Pediatrics

Background: 50% of newborns with congenital heart disease (CHD) requiring early surgery have preoperative brain injury on magnetic resonance imaging (MRI). Factors contributing to this injury are not well defined. Objective: To identify predictors of preoperative brain injury in CHD newborns.

Methods: A prospective study was performed of CHD newborns requiring CHD surgery at <1 month of age. Infants were enrolled prenatally or at ≤3 days of age. Gestational age and Apgar scores were recorded. Amplitude integrated electroencephalography (aEEG) was performed after enrollment. Blood samples were collected during the preoperative period and tested for neuronal proteins, neuron specific enolase (NSE) and S100 Beta (S100B), and for markers of oxidative stress, reduced/oxidized glutathione (GSH/GSSG) and cysteine. Preoperative brain MRI included diffusion tensor imaging which was analyzed to measure fractional anisotropy (FA) in the white matter.

Results: 10/19 infants had preoperative brain injury (white matter injury or infarcts). Infants with brain injury had a lower mean birth gestational age, 37.6±1.2 vs. 38.7±0.5 weeks, P=0.018, and a lower 1-minute Apgar score, 5.6±2.7 vs. 8.3±0.7, P=0.009. aEEG was obtained at 0.7±0.7 days of life, 11/19 (58%) were abnormal, and this was associated with brain injury on MRI (OR 8; 95%CI 1.00-63.96, P=0.049). NSE and S100B were not different preoperatively between infants with and without brain injury. Infants with brain injury had higher levels of oxidative stress (lower GSH/GSSG and cysteine/cysteine). Lower FA values (P<0.05) were measured in the corpus callosum, internal capsule, and optic radiations in infants with brain injury compared to infants without brain injury indicating reduced structural complexity.

Conclusion: A profile of biomarkers can be determined that predict preoperative brain injury in CHD newborns that can then be used in future studies of neuroprotection to improve long-term neurologic outcomes.

NS27  The Postmortem Brain Core of the COBRE Center for Psychiatric Neuroscience

Craig Stockmeier, Ph.D.
Professor, University of Mississippi Medical Center
cstockmeier@umc.edu

Craig Stockmeier, Ph.D., Gouri Mahajan, University of Mississippi Medical Center

A comprehensive understanding of the brain at the gross anatomy to the cellular and molecular level is critical to basic and clinical neuroscience. The Postmortem Brain Core, funded by NIH since 1989, has been a key resource in over 75 peer-reviewed publications. Mission: To provide high-quality: 1) human brain tissue collected at autopsy from normal control subjects and matched subjects with a psychiatric illness (e.g. major depressive disorder, schizophrenia or an alcohol or substance use disorder); 2) brain tissue from monkeys treated for 9 months with fluoxetine, an antidepressant, or vehicle; and 3) assistance to users in the selection and use of tissues related to psychiatric disorders. Psychiatric information is collected by an informant-based, structured clinical questionnaire (SCID), evaluated by a clinical team and diagnoses are determined by DSM-IV criteria.

Services: The Core provides guidance, technical support and tissue, where available, for interdisciplinary research to better understand the pathology of mental illnesses and assist faculty by enhancing competitiveness for extramural funding. There is access to limited quantities of high-quality tissue that is accompanied by a detailed psychiatric and medication history, and toxicology and neuropathology reports. Non-neurological subjects are assessed for the major mental illnesses as well as personality disorders. Services include tissue processing, celloidin embedding and sectioning, frozen sectioning, collection of cell types or tissue via LCM from cryostat sections, routine immunohistochemical and Nissl staining, and 3-D cell counting.

Support provided: Fee for Service includes access to Core equipment and/or performance of services by an investigator with the help of core manager; assistance with design and interpretation; development of new techniques. Information and a fee schedule are at: http://www.umc.edu/cpn/. Supported by P30 GM103328 and the University of Mississippi Medical Center.
NS28  Sadness, Suicide, and Drug Misuse: Results from the Youth Risk Behavior Survey

Erick Messias, M.D.
Associate Professor, University of Arkansas for Medical Sciences
emessias@uams.edu

OBJECTIVE: Suicide is a grievous and preventable tragedy, which sadly stands among the leading causes of death among teens. Previous epidemiological research has shown an association between drug use in both depression and suicidality. We hypothesized that teens reporting illicit drug or prescription drug misuse are at higher risk of depression and suicidality.

METHODS: We used data from the 2011 Youth Risk Behavior Survey (YRBS), a nationally representative sample of U.S. high school students, to study this association. Outcome variables included: reported sadness/hopelessness, suicidal ideation, planning, attempt, and attempt requiring treatment. All analyses were conducted using Stata 11. Adjusted odds ratios were calculated using logistic regression. RESULTS: 15212 questionnaires are included in our analysis. Three types of substance misuse were reported by more than 10% of U.S. high school students: cannabis (39.9% ever used), prescription drugs without a prescription (20.7% ever used), and inhalants or “huffing” described as “glue, aerosol spray, or paint” (11.4% ever used). 28.5% of students nationally reported feeling significant sadness/hopelessness in the prior 12 months lasting at least 2 weeks. This rate significantly increased to 36.5% [95% C.I. 34.7-38.4] in cannabis users, 44.4% [41.5-47.4] in prescription drug misusers, and 51.9% [49.3-54.5] in inhalant users. Regarding suicide, 7.8% of students nationally reported at least 1 attempt in the previous 12 months. This rate jumped to 12% [11.0-13.4] in cannabis users, 17% [15.2-19.5] in prescription drug users, and 23% [20.3-26.2] in inhalant users. CONCLUSION: In all suicide outcomes we found the strongest association with inhalant abuse, followed by prescription drug abuse, and then cannabis abuse. Further research is needed on prevention of drug abuse among teens. Programs to address these risk factors are recommended. Supported by NIH award P20 GM103425.

NS29  Association Between Risky Sexual Behavior and Suicidality Among Teens in the Youth Risk Behavioral Survey

Erick Messias, M.D.
Associate Professor, University of Arkansas for Medical Sciences
emessias@uams.edu

OBJECTIVE: Risky sexual behavior is a traumatic and unfortunately prevalent problem among teens. Suicide remains one of the leading causes of mortality in this age group. We hypothesized that risky sexual behavior was also a significant risk factor for suicidality among teens. METHODS: Data from the 2011 Youth Risk Behavioral Survey (YRBS) was used to study this association. The YRBS provides a nationally representative sample of 9th through 12th grade students (N = 15,212). The YRBS methodology is available at the CDC website. Potential confounders included were sex, age, and race. Adjusted odds ratios were estimated using logistic regression models. The exposures measured in this study include: onset of sexual intercourse prior to age 13, having 4 or more sexual partners, and being a self-reported victim of forced sexual intercourse. RESULTS: In a nationally representative sample of U.S. high school students, 15% reported having 4 partners or more, 8% reported being forced to have intercourse, and 6% reported debut of sexual intercourse before the age of 13. Among all US high school students 28% reported 2 week sadness. That number increased among teens with onset of sexual activity before age 13 (37%), among those who reported 4 or more sexual partners (38%) and among victims of forced sexual intercourse (59%). In the same population, 8% reported a Suicide Attempt. That number increased in those who reported 4 or more sexual partners (15%), among those who reported onset of sexual activity before age 13(23%), and among those who reported being victims of forced sexual intercourse (32%). All the associations remain statistically significant when controlling for confounders. CONCLUSION: Teens that engage in risky sexual behavior should be considered for mental health in addition to medical screening. This potentially provides a way to address depression and lower suicidality among teens. Supported by NIH award P20 GM103425.
School bullying and Cyberbullying as risk factor for suicidality among US high school students: results from the 2011 YRBS

Erick Messias, M.D.
Associate Professor, University of Arkansas for Medical Sciences
emessias@uams.edu

Erick Messias, M.D., Kristi Kindrick, M.D. University of Arkansas for Medical Sciences (University of Arkansas for Medical Sciences) Juan Castro, M.D. University of Arkansas for Medical Sciences

Introduction: Suicide in the adolescent population is a tragic and preventable cause of death, and sadly stands among the leading causes of death among teens. Recently, attention has been drawn to suicides precipitated by electronic harassment. Research looking at this relationship is in its infancy. There have been several studies linking cyberbullying to mental health problems, but not specifically addressing the extent to which it impacts suicidality. We hypothesized that subjects reporting being victims of school bullying, cyberbullying, or both, are at higher risk for depression and suicidality. Methods: We used data from the 2011 Youth Risk Behavior Surveys to study the relationship between school bullying and cyberbullying to depression and suicide. The YRBS consist of school-based, nationally representative sample (N=15,425). Students were categorized in four categories: no bullying, school bullying only, cyberbullying only, and both forms of bullying. The outcome variables included four questions addressing the continuum of suicidality: ideation, plan, attempt, and being treated for suicide. All analyses were conducted using Stata 11. Adjusted odds ratios (AOR) were calculated using logistic regressions. Results: There is a positive association of reports of depressive symptoms in victims of both types of bullying (AOR 5.4, 95% CI: (4.5-6.5)), as well as in those reporting being victim of only school bullying (2.4, (2.1-2.8)) or cyberbullying (3.4, (2.8-4.1)). There is also a positive association of suicide attempts in victims of both types of bullying (5.6, (4.4-7)), as well as those reporting being victim of only school bullying (2.3, (1.8-2.9)) or cyberbullying (3.5, (2.6-4.7)). Conclusion: Continued efforts to prevent bullying both in the school place as well as in cyberspace remain a priority in order to decrease risk of depression and suicide in adolescents.

Safety and Feasibility of transcranial magnetic stimulation (rTMS) for auditory hallucinations in schizophrenia

Erick Messias, M.D.
Associate Professor, University of Arkansas for Medical Sciences
emessias@uams.edu

Erick Messias, M.D., Mark Mennemeier, Ph.D. - University of Arkansas for Medical Sciences/CTN Edgar Garcia-Rill, Ph.D. - University of Arkansas for Medical Sciences/CTN

Introduction: repetitive transcranial magnetic stimulation (rTMS) has been approved for the treatment of major depressive episodes [1], with its potential being investigated for other neuropsychiatric disorders [2-5]. There are significant unmet needs in schizophrenia regarding the treatment of auditory hallucinations, negative symptoms, and cognitive deficits [6]. Initial evidence for the efficacy of rTMS for auditory hallucinations in schizophrenia [7-9] was followed by lingering questions about frequency and location of stimulation [3, 10-12]. The emergency of functional brain imaging also opens possibilities regarding understanding its mechanisms and more precise location. Methods: We propose a double blind, sham controlled, clinical trial comparing two locations (vertex and temporal cortex – BA22) and two frequency of stimulation (1 or 10 Hz). Analysis of resting state brain activity will be completed before and after each treatment. Results: preliminary results of four completed schizophrenia subjects demonstrate safety, tolerability and feasibility of the protocol. All subjects completed the trials without significant adverse events. Preliminary blinded data analysis shows a significant decrease in depressive symptoms (HAM-D score at start 12.5 + 1.3 versus 4.2 + 1.6 at trial end, p=.008) with no significant difference in auditory hallucinations scores (Hoffman scale 28.5 + 2.4 vs. 21 + 4.2, p=.17). Discussion: This preliminary analysis shows feasibility and safety of rTMS for auditory hallucinations. Initial results point to a robust antidepressant effects, with a possible smaller therapeutic effect for auditory hallucinations in schizophrenia. Support comes from the Center for Translational Neuroscience, University of Arkansas for Medical Sciences (P20 GM103425).
NS32  Decreased Infarct Volume in a Rabbit Ischemic Stroke Model Following Treatment with Dodecafluoropentane Emulsion

Robert D. Skinner, Ph.D.
Professor, University of Arkansas for Medical Sciences
RDSkinner@uams.edu

Robert D. Skinner, Ph.D., *Skinner, R.D.(1,2), Culp, William C.(2), Roberson, Paula K.(3), Woods, Sean D.(2), Lowery, John D.(4), Brown, Aliza (2), Borrelli, Michael J.(2) 1Neurobiology and Developmental Sciences and Center for Translational Neuroscience, University of Arkansas for Medical Sciences, Little Rock, AR 2Radiology, University of Arkansas for Medical Sciences, Little Rock, AR 3Biostatistics, University of Arkansas for Medical Sciences, Little Rock, AR 4Laboratory Animal Medicine, University of Arkansas for Medical Sciences, Little Rock, AR *Presenting author

Introduction. Dodecafluoropentane emulsion (DDFPe) absorbs and transports high levels of oxygen in vitro and in vivo. It has the potential to protect organs during hypoxic crises including hemorrhage, heart attack, cardiac and vascular surgery, coronary and carotid interventions, and stroke. Currently tPA must be given only in non-hemorrhagic cases and within 4.5 hours after onset to lyse clot. Less than 5% of patients meet these requirements. Agents that can extend this period by protecting cells in the prenumbra would allow more time for successful intervention and restitution of blood flow. In a rabbit model of ischemic stroke due to insoluble beads, we assessed the efficacy of DDFPe in decreasing infarct volume without possibility of lysis of arterial obstructions. Methods. In New Zealand white rabbits (n=40) three embolic spheres (0.7-0.9 mm dia.) were injected into the internal carotid artery. Those with only middle and/or anterior cerebral artery occlusions were accepted for testing. Rabbits were randomly assigned to groups: Control, no treatment (n=8), Immediate DDFPe (n=8), DDFPe at 30 min (n=6), 1 hr (n=7), 2 hr (n=5), and 3 hrs (n=6). DDFPe dose was 2% w/v. Intravenous injections were 0.6 ml/kg, first at the designated time and another 90 min later. Following euthanasia at 4 hrs infarct volume was determined using a vital stain on brain sections. Results. Infarct % volume means decreased for all groups: Immediate 0.75±0.69%, p=0.01; DDFP at 30 min 0.65±0.79%, p=0.02; 1 hr 1.1±0.74, p=0.04; 2 hr 0.72±0.87%, p=0.03; 3 hr 0.48±0.79, p=0.01 compared with Controls (3.31±0.69%). Discussion. DDFPe given intravenously at times immediately post-stroke to 3 hrs and analyzed at 4 hrs decreased infarct volume and protected ischemic brain tissue from hypoxia. This apparently is due to improved oxygen transport in spite of complete and permanent vessel occlusion. Clinical development may be much broader than these applications and is urgently needed.

NS33  Role of MYD88 Signaling in Ethanol Induced Immune Response in Adult Mouse Brain

Cynthia Kane, Ph.D.
Professor, University of Arkansas for Medical Sciences
kanecynthiaj@uams.edu

Cynthia Kane, Ph.D., Kevin D. Phelan James C. Douglas Gail Wagoner Jennifer Johnson P.D. Drew

Recent studies demonstrated that excessive alcohol consumption can result in brain inflammation. A series of elegant studies by the Guerri laboratory demonstrated that toll-like receptor (TLR) 4 plays a critical role in ethanol induced inflammation in the brain. TLR4 is known to activate two distinct signaling pathways, the MyD88-dependent pathway and the MyD88-independent or TRIF pathway. In the current study, we demonstrate that ethanol treatment (6 g/kg, 15% w/v, split dose) of adult C57BL/6 mice resulted in increased expression of mRNAs encoding the chemokine MCP-1 and the cytokine IL-6. The expression of MCP-1 mRNA was increased following ethanol treatment in all brain regions evaluated (hippocampus, cerebellum, and cortex), while IL-6 expression was increased only in the cerebellum. Importantly, we observed that ethanol induction of these pro-inflammatory molecules was not observed in MyD88 knock-out mice (on a C57BL/6 genetic background) demonstrating a critical role of MyD88 in ethanol induced brain inflammation. Recent studies have also demonstrated that MCP-1 and MyD88 are important modulators of alcohol drinking behavior. Thus, the current studies support an important link between alcohol induced brain inflammation and addiction to alcohol. Understanding the mechanisms by which alcohol induces neuroinflammatory events will be important in developing novel therapies designed to block alcohol addiction and alcohol induced brain toxicity.
A paradigm shift has resulted from recent studies indicating that alcohol abuse is associated with inflammation in the brain. Interestingly, these studies suggest that expression of these inflammatory molecules in the brain is linked to alcohol addiction. Our previous studies in the neonatal rodent brain indicate that ethanol is not only toxic to neurons, but is also toxic to microglia, the innate immune cells in the CNS. Our studies using co-culture of cerebellar granule neurons and microglia indicate that microglia are constitutively neurotrophic and protect against ethanol pathogenesis. In both paradigms, ethanol appears to convert microglia from a quiescent phenotype to an activated phenotype characterized by production of inflammatory molecules. These studies suggest that ethanol alters normal interactions between neurons and microglia. In the present study we treated adolescent and adult animals with ethanol and investigated changes in MCP-1, IL6, IL1-β, TNF-α, COX-2, NOX-2, and iNOS mRNA in the cerebellum, cerebral cortex, and hippocampus. Expression varies depending on the age of the animal, the brain region, and the specific molecule. It is interesting that ethanol induces MCP-1 expression in each brain region differentially at each age. Since MCP-1 has previously been demonstrated to alter alcohol consumption, these studies support a link between inflammation and alcohol addiction. This study also reveals that ethanol increases microglial and astrocyte staining with Iba-1 and GFAP respectively in selected brain regions. Together, the changes in cytokines, chemokines, and microglial and astrocyte staining suggest partial glial activation occurs in adolescent and adult animals in response to ethanol. Understanding the mechanisms by which ethanol induces neuroinflammatory events will be important in developing novel neuroprotective therapies designed to block the toxic effects of alcohol.
NS36

Does daily kangaroo care provide sustained pain & stress relief in preterm infants?

Anita Mitchell Ph.D.
Clinical Associate Professor, University of Arkansas for Medical Sciences (UAMS)
AMitchell@uams.edu

Anita Mitchell Ph.D., Charlotte Yates Ph.D., University of Central Arkansas David Keith Williams Ph.D., University of Arkansas for Medical Sciences, Dept of Biostatistics Richard Whit Hall M.D., University of Arkansas for Medical Sciences, Dept of Neonatology

Purpose: 1. Determine whether stress in preterm infants, measured with salivary cortisol levels, is reduced after five days of Kangaroo Care (KC) compared to five days of Standard Care (SC). 2. Determine whether kangaroo care provides sustainable pain relief beyond the immediate period of skin-to-skin holding. Methods: Preterm infants (n=38) born at 27-30 weeks gestational age were randomized to two groups and received either KC or SC starting on day of life (DOL) five and continuing through DOL nine. Salivary cortisol was measured on DOL five and again on DOL ten. Repeated measures ANOVA and t tests were used to analyze differences between the two groups. Pain during nasal suctioning over the five days was assessed using the Premature Infant Pain Profile (PIPP). Results: 1. Sufficient saliva for analyzing salivary cortisol was collected for 13 KC infants and 11 SC infants. There was no main effect of group (p=0.49), but there was a significant main effect of age (DOL five versus DOL ten), with salivary cortisol levels decreasing in both groups over the five days (p=0.02). 2. Pain scores for both groups (n=38) indicated mild to moderate pain during suctioning. There was no significant difference in pain scores between groups. Conclusion: 1. KC did not affect salivary cortisol levels in preterm neonates, but levels in both the KC and SC groups decreased over time from DOL five to DOL ten. 2. Infants may require pain management during routine suctioning.

NS37

Docking studies on Leonotis leonurus and Leonurus cardiaca derived compounds for their potential activity at CB1

Veena Gadepalli
Graduate Student, University of Mississippi
vgadepal@go.olemiss.edu

Veena Gadepalli, Pankaj Pandey, Kuldeep K. Roy, Robert J. Doerksen, Ilias Muhammad

The endocannabinoid system is made up of a group of endogenous lipids (endocannabinoids) and their receptors along with enzymes that regulate synthesis and degradation of these endocannabinoids. Cannabinoid receptors are G protein-coupled receptors that play important roles in many bodily processes such as bone growth, pain, immune function and metabolism through interaction with endocannabinoids; modulating activity of the endocannabinoid system therefore has clinical importance. There are two types of cannabinoid receptors in mammals, cannabinoid receptor 1 (CB1) and cannabinoid receptor 2 (CB2), which can be targeted either through agonist or antagonist activity. In this project, a number of compounds reported from the plant species Leonotis leonurus and Leonurus cardiaca were docked with the CB1 receptor. These plants are said to have effects similar to Cannabis. The majority of the isolated compounds are diterpenoids (some analogous to salvia diterpenoids) and some are alkaloids. Docking was performed using the Glide module of the Schrödinger suite with the CB1 receptor model being an in house homology model developed from a bovine rhodopsin template in the Doerksen lab. The major ligand-binding site of CB1 is located near the Lys192 (Lys3.28) residue. With the docking center specified as Trp279 (Trp5.43), the binding modes of these compounds were analyzed. Through this study, we attempt to identify the potential ligand(s) that may demonstrate the physiological benefits of cannabinoids. Towards this goal, we report on a detailed docking analysis of the 3D-interactions of the plant-derived compounds with the CB1 receptor.
NS38  Novel benzopyran and benzofuran scaffolds targeting the cannabinoid receptors

Eric Bow
Graduate Student, Department of Medicinal Chemistry, University of Mississippi
ebow@go.olemiss.edu

Eric Bow, Dr. John Rimoldi, Department of Medicinal Chemistry, University of Mississippi

Cannabinoids have been shown to possess potent analgesic and anti-inflammatory properties in addition to their well-known psychotropic effects. There are two characterized cannabinoid receptors, CB1 and CB2. While both receptors are expressed abundantly in the central and peripheral nervous systems, CB2 is also found in the immune system and gastrointestinal tract. CB1 is largely associated with the psychotropic effects of non-selective cannabinoids, whereas selective CB2 agonism seems to be devoid of these properties. We sought to develop CB2 selective agonists based on novel benzofuran and benzopyran scaffolds. The synthesis of substituted 6-alkyl-benzofurans and substituted 7-alkyl-benzopyrans is presented.

NS39  Novel treatment for schizophrenia

E. Garcia-Rill, Ph.D.
SMDonofrio@uams.edu

E. Garcia-Rill, S. D’Onofrio1, N. Kezunovic1, F.J. Urbano2, E. Messias1, E. Garcia-Rill1 1Center for Translational Neuroscience, Dept. Neurobiology & Dev. Sci. University of Arkansas for Medical Sciences, Little Rock, AR and 2 IFIBYNE- CONICET, University of Buenos Aires, Argentina

Neuronal calcium sensor protein (NCS-1) has been found to be overexpressed in the brains of schizophrenic and bipolar patients but not depressed patients or controls. We discovered that almost all cells in the reticular activating system (RAS), especially the pedunculopontine nucleus (PPN), fire maximally at gamma band frequencies and that such activity is subserved by subthreshold membrane oscillations due to high threshold, voltage-dependent N- and P/Q-type calcium channels. Using patch clamp recordings in 9-13 day rat brainstem slices, we found that NCS-1 (in the recording pipette) at low levels (1 uM) increased the frequency and amplitude of membrane oscillations induced by current ramps or by the nonspecific cholinergic agonist carbachol (CAR). In contrast, high levels (10 uM) of NCS-1 were found to block gamma band oscillations in PPN neurons, but exposure to the stimulant modafinil (MOD, 300 mM) were found to restore oscillations in the presence of high levels of NCS-1. These findings suggest that, a) NCS-1 at low levels potentiates gamma band activity in the PPN, b) NCS-1 at high levels blocks gamma band oscillations in the PPN, c) NCS-1 overexpression may be responsible for the decrease in gamma band activity in schizophrenia, and d) MOD restored gamma band activity under high levels of NCS-1, suggesting a novel treatment for schizophrenia.
Characterization of beta amyloid clearance by mouse cortical astrocytes

Yazan Batarseh
Graduate Student, College of Pharmacy, University of Louisiana at Monroe
batarsy@warhawks.ulm.edu

Yazan Batarseh, College of Pharmacy, University of Louisiana at Monroe, Yazan Batarseh; College of Pharmacy, University of Louisiana at Monroe, Dr. Amal Kaddoumi; College of Pharmacy, University of Louisiana at Monroe

Alzheimer’s disease (AD) is a neurodegenerative disorder characterized by synaptic loss and neuronal death. While the exact etiology of AD is unknown there is increasing bulk of evidence that the main pathological process involved is related to faulty CNS clearance of beta amyloid (Aβ). Astrocytes role in AD is crucial because they possess the ability to clear Aβ from the brain by active uptake and degradation and/or by transporting Aβ from brain parenchyma to the perivascular space and consequent Aβ clearance to the blood stream across the blood brain barrier (BBB). The aim of this study is to investigate the exact role of astrocytes in Aβ clearance, which may anchor the basis of a new therapeutic approach for AD treatment. Primary astrocytes isolated from mice brain cortex were used to accomplish this aim. Initial characterization using western blot demonstrated the expression of Aβ transport proteins and degrading enzymes including P-glycoprotein (P-gp), low-density lipoprotein receptor-related protein 1 (LRP1), insulin degrading enzyme (IDE) and neprilysin, in addition to CNS lipidation contributors such as ABCA1 and ApoE. To our knowledge, this is the first study to show P-gp expression in astrocytes using western blot. Uptake studies with 125I- Aβ40 showed that astrocytes rapidly uptake Aβ with approximately 50% degradation capacity. Further studies are currently in progress to investigate the contribution of astrocytes to the clearance process of Aβ that will be discussed in the poster.

The fine temporal structure of the rat licking pattern: What causes the variability in the interlick intervals?

Xiong Bin Lin
Graduate Student, University of Arkansas for Medical Sciences
amhayar@uams.edu

Xiong Bin Lin, Center for Translational Neuroscience, Dept. of Neurobiology and Developmental Sciences, Univ. of Arkansas for Medical Sciences, Xiong Bin Lin, Center for Translational Neuroscience, Dept. of Neurobiology and Developmental Sciences, Univ. of Arkansas for Medical Sciences, Dwight R. Pierce, Dept. of Pharmaceutical Sciences, Univ. of Arkansas for Medical Sciences; Kim Edward Light, Dept. of Pharmaceutical Sciences, Univ. of Arkansas for Medical Sciences; Abdallah Hayar, Center for Translational Neuroscience, Dept. of Neurobiology and Developmental Sciences, Univ. of Arkansas for Medical Sciences

Licking is a repetitive behavior controlled by a central pattern generator. Even though interlick intervals (ILI) within bursts of licks are considered fairly regular, the conditions that affect their variability are unknown. We analyzed the licking pattern in rats that licked water, 10% sucrose solution, or 10% ethanol solution, in 90 min recording sessions after 4 h of water deprivation. The histograms of ILIs indicate that licking typically occurred at a preferred ILI of about 130-140 ms with evidence of bi- or multi-modal distributions due to occasional licking failures. We found that the longer the pause between bursts of licks, the shorter was the first ILI of the burst. When bursts of licks were preceded by a pause >4 sec, the ILI was the shortest (~110 ms) at the beginning of the burst and then it increased rapidly in the first few licks and slowly in subsequent licks. Interestingly, the first ILI of a burst of licks was not significantly different when licking any of the 3 solutions, but subsequent licks exhibited a temporal pattern characteristic of each solution. The rapid deceleration in intraburst licking rate was due to an increase from ~27 ms to ~56 ms in the tongue-spout contact duration while the intercontact interval was only slightly changed (80-90 ms). Therefore, the contact duration seems to be the major factor that increases the variability in the ILIs, and could be another means for the rat to adjust the amount of fluid ingested in each individual lick. Support: Grant P20 GM103425-09.
NS42 Change in risk perception among parents of ATV users

Taylor House
Graduate Student, University of Arkansas for Medical Sciences
mullinssamanthah@uams.edu

Taylor House, Samantha Mullins (University of Arkansas for Medical Sciences) Beverly Miller (University of Arkansas for Medical Sciences) Mary E. Aitken (University of Arkansas for Medical Sciences)

Background: All-terrain vehicles (ATVs) are ever increasing in popularity with the Consumer Product Safety Commission (CPSC) estimating that 10.7 million four-wheel ATVs were in use in 2011. This popularity of use results in a large number of associated injuries, particularly in child and adolescent populations. Therefore, an effective means of education regarding the dangers associated with children riding and/or operating ATVs is greatly needed, but little research has been done in this area. This study sought to address this problem in the parental population through the use of ATV crash simulations and animations. The aims of this study were to 1) determine if ATV crash simulations were a successful means of shifting parental risk perception regarding ATV use and 2) determine which crash scenario (animation vs. simulation) appealed to a broader audience. Method: Utilizing the Health Belief Model, a pre/post intervention survey was constructed which assessed parent’s perception of risk, child’s riding behaviors, impact of conflicting safety messaging, perceived susceptibility and perceived safety. The intervention involved the viewing of a video that included simulated and animated ATV crashes with six and ten year olds riding an adult sized ATV. The survey was administered to parents/guardians presenting to the Arkansas Children’s Hospital Emergency Department of children under the age of 18 who had ridden an ATV in the last year. Data were collected and managed using REDCap electronic data capture tools hosted at Arkansas Children’s Hospital. Results: 258 families were approached and 100 parents completed the survey. Data analysis is ongoing. Conclusion: Data analysis will continue in order to determine the statistical success of the study. However, encouraging comments were received from participants alluding to the success of the video simulations and animations in educating the target population.

NS43 Involvement of P-glycoprotein in the Hepatobiliary Disposition and Blood Brain Barrier Transport of Tacrine

Loqman A. Mohamed
Graduate Student, College of Pharmacy, Department of Basic Pharmaceutical Sciences, University of Louisiana at Monroe
mohamela@warhawks.ulm.edu

Loqman A. Mohamed, Amal Kaddoumi, University of Louisiana at Monroe

The knowledge of disposition kinetics of tacrine, a first choline esterase inhibitor approved by FDA for the treatment of Alzheimer’s disease (AD), would help to understand its hepatotoxicity, its therapeutic effect, and improve the management of patients with AD. Hence, the current study aims to characterize tacrine transport kinetics and identify the possible role of P-glycoprotein (P-gp) in mediating tacrine transport through the liver and the blood brain barrier (BBB). Sandwich-cultured primary rat hepatocytes (SCHs) and RBE4 cells were used to accomplish this aim. Tacrine uptake in SCHs was saturable and showed involvement of carrier-mediated process with apparent Km, 31.5µM and Vmax, 908pmol/min/mg protein. Verapamil showed a concentration dependant inhibition of tacrine sinusoidal uptake with 3-fold reduction at 100µM indicating a possible role of organic cation transporters (OCTs). Biliary excretion index (BEI%) of tacrine was maximum at 10min with 22.9±1.9% which was decreased by 60% with 5µM valspodaor indicating the involvement of canalicular P-gp. This function was also confirmed at the BBB using RBE4 cells as a model, where efflux of tacrine was saturable and uptake of 1µM tacrine was enhanced by P-gp inhibition with 5µM elacridar by 3-fold. Amyloid beta (Aβ), a hallmark of AD, is a P-gp substrate and its uptake was increased by 40% when co-incubated with 500µM tacrine in RBE4 cells. Western blot analysis of 48h tacrine treated RBE4 down-regulated P-gp and up-regulated low density lipoprotein-receptor related protein-1 (LRP1) and receptor for advanced glycation end products (RAGE) and was reflected on 125I-Aβ40 uptake, enhanced by 35%. Collectively, our results show that tacrine hepatobiliary disposition is mediated by sinusoidal OCTs and canalicular P-gp. Besides, tacrine treatment decreases the expression of P-gp and up-regulates LRP1 and RAGE, which may affect Aβ clearance across the liver and BBB and influence Aβ systemic and brain homeostasis.
NS44  Characterization of amyloid-β cerebral clearance across mouse and human blood-brain barrier models

Hisham Qosa
Graduate Student, College of Pharmacy, University of Louisiana at Monroe
qosahh@warhawks.ulm.edu

Hisham Qosa, College of Pharmacy, University of Louisiana at Monroe, Hisham Qosa; College of Pharmacy, University of Louisiana at Monroe, Bilal S. Abuasal; College of Pharmacy, University of Louisiana at Monroe. Ignacio A. Romero; The Open University, Life Sciences, Milton Keynes, UK. Babette Weksler; Weill Medical College, Medicine/Heme-Onc, New York, NY, USA. Pierre-Oliver Couraud; INSERM U1016, Institut Cochin, Paris, France. Jeffrey N. Keller; Pennington Biomedical Research Center, Louisiana State University. Amal Kaddoumi; College of Pharmacy, University of Louisiana at Monroe.

Accelerated cerebral accumulation of amyloid-β peptides (Aβ) in Alzheimer’s disease has been related to its faulty clearance. Efflux across blood-brain barrier (BBB) and brain degradation mediate efficient Aβ clearance preventing its accumulation. However, the contribution of each process to the brain clearance of Aβ remains unclear. Using a modified form of the brain efflux index method, we estimated that 62% of intracerebrally injected 125I-Aβ40 is cleared across BBB while 38% is cleared by brain degradation. Given the significant contribution of BBB to brain Aβ40 clearance, kinetic studies for Aβ40 disposition in bEnd3 and hCMEC/D3 cells, representative in vitro mouse and human BBB models, respectively, were performed to compare Aβ40 clearance rates between the two models. Expression studies showed both cells to express different levels of P-glycoprotein and RAGE, while LRP1 levels were comparable. Activity studies demonstrated 30-fold higher rate of 125I-Aβ40 uptake and 15-fold higher rate of degradation by bEnd3 compared to hCMEC/D3 cells. Finally, we established a mechanistic model, which could successfully predict cellular levels of 125I-Aβ40 and the rate of each process. The mechanistic model showed significantly higher rates of uptake and degradation in bEnd3 explaining the differences in 125I-Aβ40 disposition between mouse and human BBB models.

NS45  Emerging arylcyclohexylamine drugs of abuse: drug discrimination, locomotor activity and thermoregulation

William S. Hyatt
Graduate Student, University of Arkansas for Medical Sciences
WSHyatt@uams.edu

William S. Hyatt, Brenda M Gannon, University of Arkansas for Medical Sciences Jonathan Bauer-Erickson, Hendrix College Andrew P Norwood, University of Arkansas for Medical Sciences William D Wessinger, University of Arkansas for Medical Sciences William E. Fantegrossi, University of Arkansas for Medical Sciences

In recent years, extensive internet availability of a range of “research chemicals” has lead to the emergence of new compounds as drugs of abuse, including arylcyclohexylamine analogues of the NMDA receptor antagonist phencyclidine (PCP). One of the most prevalent of these compounds, methoxetamine (MXE), was compared to the structurally similar arylcyclohexylamines phencyclidine (PCP), eticyclidine (PCE) and tenocyclidine (TCP) in rodents. First, PCP was established as a discriminative stimulus in rats. Once discrimination was established, substitutions were performed with various doses of PCP, eticyclidine (PCE), tenocyclidine (TCP) or the negative control compounds morphine and JWH-018 using a cumulative dosing procedure. PCP, MXE, PCE and TCP dose-dependently and fully substituted for the PCP training dose, while morphine and JWH-018 occasioned responding primarily on the saline-appropriate lever up to doses that suppressed response rates. Next, these same rats were implanted with osmotic mini-pumps to elicit PCP dependence. Suppression of response rates in a food-maintained operant task were used as an index of withdrawal when the pumps were removed after 10 days. Increasing doses of MXE restored normal behavior in PCP-dependent rats. Finally, mice were implanted with biotelemetry probes to simultaneously assess core temperature and locomotor activity in response to increasing doses of PCP, PCE, TCP or MXE. All compounds produced locomotor stimulant effects and elicited hypothermia. In all cases, MXE was more potent than PCP. These results suggest that novel arylcyclohexylamine drugs of abuse are likely to be more potent than human users of these emerging drugs might expect, perhaps leading to overdose if they base their doses on PCP. Future directions of this experiment include the testing of novel emerging PCP analogues, such as methoxetamine and 3-methoxyeticyclidine. This work supported by RR020146, RR029884, and by an ASPET SURF award to JBE.
**NS46**  
**In vivo effects of synthetic cannabinoids JWH-018 and JWH-073 versus Δ9-THC: inhalation versus intraperitoneal injection**

Ramey L. Marshall  
Graduate Student, University of Arkansas for Medical Sciences  
RMARSHELL@uams.edu

Ramey L. Marshall, William S Hyatt, University of Arkansas for Medical Sciences  
Sarah M Zimmerman, University of Arkansas for Medical Sciences  
William E Fantegrossi, University of Arkansas for Medical Sciences

Synthetic cannabinoids have recently emerged as popular drugs of abuse in the US. These products are presumed to possess pharmacological properties similar to Δ9-tetrahydrocannabinol (Δ9-THC), the primary psychoactive constituent of marijuana. Although structurally different from Δ9-THC, these synthetic compounds bind to and activate cannabinoid CB1 receptors. Although humans typically consume these compounds by smoking them, preclinical studies, to this point, have relied on injection for drug delivery. We used the cannabinoid tetrad assay in mice to compare in vivo effects of inhaled drugs with injected doses of two common synthetics, as well as with Δ9-THC. Mice inhaled various doses of Δ9-THC, JWH-018, or JWH-073 using a whole body exposure system, or were injected intraperitoneally (IP) with these same compounds. We then compared the observed induced cannabimimetic effects via the tetrad assay: rectal temperature, tail flick latency in response to radiant heat, horizontal bar catalepsy, and suppression of locomotor activity. JWH-018 and JWH-073 elicited Δ9-THC-like effects across both routes of administration, and effects following inhalation were attenuated by pretreatment with the CB1 antagonist, rimonabant. Interestingly, no cataleptic effects were observed following inhalation, but all compounds induced catalepsy following injection. Synthetic cannabinoids JWH-018 and JWH-073 elicit dose-dependent, CB-1 receptor-mediated Δ9-THC-like effects in mice when delivered via inhalation or via injection, but with evidence of increased potency, compared to Δ9-THC, supported by observations seen in hypothermia, analgesia, and locomotor suppression. Across these routes of administration, differences in cataleptic effects may implicate the involvement of active metabolites of these compounds. This research supported by the University of Arkansas for Medical Sciences Center for Translational Neuroscience (RR020146) and the University of Arkansas for Medical Sciences Translational Research Institute (RR029884).

**NS47**  
**Monoamine transporter mediated in vivo effects of abused “bath salt” constituent MDPV in mice**

Brenda M. Gannon  
Graduate Student, University of Arkansas for Medical Sciences  
BMGannon@uams.edu

Brenda M. Gannon, Kenner C Rice, NIDA/NIAAA, Bethesda, M.D. USA  
Sarah M Zimmerman, University of Arkansas for Medical Sciences  
William E Fantegrossi, University of Arkansas for Medical Sciences

In recent years, synthetic analogues of naturally-occurring cathinone in commercial “bath salt” preparations have emerged as psychostimulant-like drugs of abuse. 3,4-Methylenedioxyxypovalerone (MDPV) is a common constituent of these illicit products, and recent in vitro studies implicate monoamine transporters as mediators of its pharmacological effects. In these studies, adult male NIH Swiss mice were trained to discriminate MDPV from saline, and a range of substitution doses of MDPV, MDMA and METH were then assessed. In separate groups of mice, surgically-implanted radiotelemetry probes simultaneously monitored thermoregulatory and locomotor responses to various doses of MDPV and MDMA, as a function of ambient temperature. The role of monoamine transporters in these effects were assessed via pretreatment with the non-selective transporter inhibitor imipramine, the serotonin-selective reuptake inhibitor fluoxetine, the norepinephrine-preferring reuptake inhibitor desipramine, or saline, followed by MDPV. We found that mice reliably discriminated the MDPV training dose from saline, and that cumulative doses of MDPV, MDMA, and METH all fully substituted for the MDPV training stimulus with similar ED50 values. Stimulation of motor activity was observed following administration of a wide range of MDPV doses (1 to 30 mg/kg), and the warm ambient temperature potentiated motor activity and elicited profound stereotypy and self-injurious behavior at 30 mg/kg. In contrast, similar MDPV-induced hyperthermic effects were observed in both the cool and warm ambient environments. These studies suggest that while the interoceptive effects of MDPV are similar to those of MDMA and METH, direct effects on thermoregulatory processes and locomotor activity are likely mediated by different mechanisms than those of MDMA. This work supported by RR020146 and RR029884.
NS48  
Effects of neonatal visceral pain on morphine tolerance, dependence, and withdrawal in rats

Andrew P. Norwood  
Graduate Student, University of Arkansas for Medical Sciences  
APNorwood@uams.edu

Andrew P. Norwood, William E Fantegrossi, University of Arkansas for Medical Sciences

Changes in brain opioid systems have been demonstrated in response to neonatal visceral pain (NVP), but few studies have examined the impact of these changes on opioid pharmacology. In these studies, we examined the effects of NVP on the development of tolerance, dependence, and expression of withdrawal effects of morphine in the rat. Experimental rats were subjected to a colorectal distension procedure on postnatal days 4, 6, and 8 to induce NVP, while control rats were not exposed to the NVP procedure. All rats were gradually shaped to a terminal FR20 schedule reinforced by food presentation. Once responding was stable and reliable, saline was injected subcutaneously (SC) before behavioral sessions, and morphine was administered (SC) immediately after behavioral sessions. Morphine doses were increased one quarter-log every 7 days, from 1.0 mg/kg, to a final dose of 30 mg/kg, upon which rats were maintained for the duration of the experiment. Various doses of the opioid antagonist naltrexone (NTX) were sometimes administered 10 min before behavioral sessions to precipitate withdrawal. For both groups of rats, NTX dose-dependently suppressed response rates, indicative of a precipitated withdrawal effect on food-maintained responding. However, NTX induced more pronounced rate suppression in NVP rats at all tested doses. These findings demonstrate that the changes in brain opioid systems elicited by NVP have persistent pharmacological consequences into adulthood, are consistent with our previous studies suggesting that NVP increases sensitivity to abuse-related effects of opioids across development, and extend our characterization of this vulnerable phenotype to include an increased susceptibility to antagonist-precipitated withdrawal. These studies supported by the University of Arkansas for Medical Sciences Center for Translational Neuroscience (RR020146) and the University of Arkansas for Medical Sciences Translational Research Institute (RR029884).

NS49  
Visualizing P/Q- and N-type calcium channels in the pedunculopontine nucleus

Brennon Luster  
Graduate Student, University of Arkansas for Medical Sciences  
BRLuster@uams.edu

Brennon Luster, B. Luster1, J. Hyde1, F.J. Urbano2, and E. Garcia-Rill1, 1Center for Translational Neuroscience, University of Arkansas for Medical Sciences, Little Rock, AR, US and 2IFIBYNE-CONICET, University of Buenos Aires, Argentina.

The pedunculopontine nucleus (PPN) is involved in waking and paradoxical sleep as part of the reticular activating system. Every PPN cell fires maximally at gamma band. Previous studies showed that this activity is due to P/Q- and N-type calcium channels. The purpose of this study was to confirm that the wide field fluorescent calcium signal in the cell as a whole is mainly due to P/Q-type channels and only partially due to N-type calcium channels. These studies also compared two custom LED illumination systems. Responses were recorded using patch clamp electrodes in 9-16 day old sagittal rat brain slices. Slices were recorded at 37°C perfused with oxygenated aCSF containing the synaptic blockers gabazine (GABA antagonist), strychnine (glycine antagonist), 6-cyano-7-nitroquinoxaline-2,3-dione (AMPA/kainate receptor antagonist), APV (NMDA receptor antagonist), and TTX to block sodium channels. Recording electrodes also contained Oregon Green BAPTA 1 (OGB1). Calcium transients were visualized using a wide field high sensitivity electron-multiplying camera. Images of the whole cell from eight ramps were averaged to produce the final calcium image series for each cell. Four illumination systems were compared. Cells (n=24) generated calcium signals in both the soma and dendrites. Fluorescent calcium signals were completely blocked with a combination of of ω-Agatoxin-IVA (AgA), a specific P/Q-type calcium channel blocker, and ω-conotoxin-GVIA (CgTx), a specific N-type calcium channel blocker. Calcium signals were mostly blocked when AgA was used by itself. This study demonstrated that the fluorescent calcium signal of the cells is mainly due to P/Q-type voltage-gated calcium channels and only minimally due to N-type voltage-gated calcium channels. This was made possible by the use of a stable, low noise LED illumination system and high sensitivity camera.
NS50  
**Calcium mediated sub-threshold oscillations in the pedunculopontine nucleus using a novel ratiometric imaging technique**

James Hyde  
Graduate Student, University of Arkansas for Medical Sciences  
JHyde@uams.edu

**James Hyde, J. Hyde1, F.J. Urbano2, and E. Garcia-Rill1, 1Center for Translational Neuroscience, University of Arkansas for Medical Sciences, Little Rock, AR, US and 2 IFIBYNE-CONICET, University of Buenos Aires, Argentina.**

The pedunculopontine nucleus (PPN) is a component of the reticular activating system, and is involved in waking and paradoxical sleep. Gamma oscillations are present in all PPN neurons and are mediated by N- and P/Q-type calcium channels. We tested the hypothesis that high-speed calcium imaging would reveal calcium-mediated oscillations in synchrony with patch clamp recorded oscillations during depolarizing current ramps. This study also characterized cellular sub-domains using a novel ratiometric technique of Oregon Green BAPTA-1 (OGB1) coinjected with a new long-stokes-shift dye, Chromeo 494 (CHR). Using patch clamp electrodes, slices were recorded at 37°C perfused with oxygenated aCSF containing the synaptic blockers gabazine (GABAA antagonist), strychnine (glycine antagonist), 6-cyano-7-nitroquinoxaline-2,3-dione (AMPA/kainate receptor antagonist), and APV (NMDA receptor antagonist), and also Tetrodotoxin to block sodium channels. Recording electrodes also contained Fura-2, Bis Fura-2, or OGB1/CHR calcium sensitive dye. Calcium transients were visualized using a high speed, dual camera imaging system. Cells manifested calcium transients with oscillations in both somatic and proximal dendrite fluorescence recordings. Fluorescent calcium transients were blocked with the nonspecific calcium channel blocker, cadmium, or the combination of ω-Agatoxin-IVA (AgA), a specific P/Q-type calcium channel blocker, and ω-conotoxin-GVIA (CgTx), a specific N-type calcium channel blocker. Overlaying calcium and electrical recordings showed highly coincident oscillation peaks suggesting the presence of distributed oscillatory sub-domains. This study showed that high-speed calcium imaging is a viable method for measuring sub-threshold calcium oscillations with high spatial and temporal resolution in cellular sub-domains. The OGB1/CHR ratiometric indicator proved comparable to traditional calcium indicators for accuracy while allowing high-speed image acquisition.

NS51  
**Effect of Modafinil on P/Q-type calcium channel-dependent oscillations in the PPN**

Stasia D’Onofrio  
Graduate Student, University of Arkansas for Medical Sciences  
SDonofrio@uams.edu

**Stasia D’Onofrio, S. D’Onofrio1, N. Kezunovic1, F.J. Urbano2, E. Garcia-Rill1 1Center for Translational Neuroscience, Dept. Neurobiology & Dev. Sci. University of Arkansas for Medical Sciences, Little Rock, AR and 2 IFIBYNE- CONICET, University of Buenos Aires, Argentina**

The pedunculopontine nucleus (PPN) is a component of the reticular activating system, and is involved in waking and paradoxical sleep. Gamma oscillations are present in all PPN neurons and are mediated by high threshold voltage-dependent N- and P/Q-type calcium channels. We tested the hypothesis that the stimulant Modafinil (MOD) would modulate gamma band oscillations in PPN neurons activated by the nonspecific cholinergic agonist Carbachol (CAR). Whole-cell patch-clamp responses were recorded on 9-13 day old rat brainstem slices. Slices were recorded at 370C perfused with oxygenated aCSF in an immersion chamber containing the synaptic blockers gabazine (GABAA antagonist), strychnine (glycine antagonist), 6-cyano-7-nitroquinoxaline-2,3-dione (AMPA/kainate receptor antagonist), APV (NMDA receptor antagonist), and mecamylamine (nicotinic receptor blocker), and also Tetrodotoxin to block sodium channels. CAR and MOD were used to study changes in P/Q-type calcium channel-dependent oscillator behavior of PPN neurons. We found that persistent application of MOD did not change the frequency or amplitude of 1 sec ramp-induced oscillations (n=13; p=0.31). However, when CAR was added together with MOD, both the frequency (n=10; p=0.01) and the amplitude (n=14; p<0.05) of the oscillations increased at gamma frequencies, compared to the control condition without CAR and MOD. We found that frequency of oscillations after CAR+MOD (35.7±3 Hz) was significantly lower than with CAR alone (47.5±2 Hz) (n=27; p=0.001). However, the amplitude of the oscillations at gamma range (30-60 Hz) during persistent application of CAR (2±1 mV2/Hz), was significantly lower than during CAR+MOD (9.4±4 mV2/Hz) application (n=27; p=0.007). These results suggest that, while MOD by itself had no significant effect on gamma oscillations in PPN neurons. When exposed to persistent application of CAR, MOD increased the amplitude but decreased the frequency of ramp-induced oscillations.
Muscarinic modulation of gamma band activity in the pedunculopontine nucleus (PPN)

N. Kezunovic
Graduate Student, University of Arkansas for Medical Sciences
NKezunovic@uams.edu

N. Kezunovic 1, J. Hyde1, B. Goitia2, V. Bisagno2, F.J. Urbano2, E. Garcia-Rill1 1Center for Translational Neuroscience, Dept. Neurobiology & Dev. Sci. University of Arkansas for Medical Sciences, Little Rock, AR and 2 IFIBYNE- CONICET, University of Buenos Aires, Argentina

The pedunculopontine nucleus (PPN) is part of the reticular activating system, and receives cholinergic input. We reported that persistent application of the nonspecific cholinergic agonist carbachol (CAR) increased the frequency of oscillatory activity in PPN neurons, which is dependent on P/Q-type calcium channels. We tested the hypothesis that M2 muscarinic receptors and G-proteins mediate the increase in CAR-induced oscillatory frequency in PPN cells. Patch-clamp responses were recorded on 9-13 day old rat brainstem slices at 370C perfused with oxygenated aCSF containing the synaptic blockers gabazine (GABAA antagonist), strychnine (glycine antagonist), 6-cyano-7-nitroquinoxaline-2,3-dione (AMPA/kainate receptor antagonist), APV (NMDA receptor antagonist), mecamylamine (nicotinic receptor blocker), and TTX to block sodium channels. Acute application of CAR blocked oscillations through M2 muscarinic receptors (blocked by the M2 antagonist pirenzepine, but not the M1 antagonist methotrime), an effect reversed with atropine. However, persistent application of CAR increased the frequency of ramp-induced oscillatory activity in PPN neurons through M2 receptors [40±1Hz (CAR) vs 23±1Hz (without CAR); p<0.001]. We then tested the effects of the G-protein antagonist guanosine 5’-[b-thio] diphosphate trilithium salt (GDP-b-S), and the G-protein agonist 5’–[g-thio] triphosphate trilithium salt (GTP-g-S). We found that the increase in the frequency of oscillations induced by M2 cholinergic receptors was dependent on a voltage-independent G-protein mechanism. These results suggest that short-lasting cholinergic input to the PPN results in inhibition of high frequency activity. However, persistent cholinergic input is mediated by G-proteins that otherwise would inactivate high threshold, voltage-dependent calcium channels.

Mechanism of leptin action on arousal

P. Beck
Graduate Student, University of Arkansas for Medical Sciences
PBBeck@uams.edu

P. Beck1, P. Beck1, F.J. Urbano2, E. Garcia-Rill1 1Center for Translational Neuroscience, Dept. Neurobiology & Dev. Sci. University of Arkansas for Medical Sciences, Little Rock, AR and 2 IFIBYNE- CONICET, University of Buenos Aires, Argentina

Leptin regulates appetite and energy and is increased in obese individuals, although these individuals often exhibit leptin resistance. Obesity is characterized by sleep/wake disturbances in the absence of sleep-disordered breathing. Arousal and REM sleep are regulated by the cholinergic arm of the reticular activating system, the pedunculopontine nucleus (PPN). The goal of this project is to determine the intracellular mechanism of leptin in the PPN, and thus the possible link between obesity and related sleep disorders. We thus investigated the intracellular mechanisms by which leptin may act on PPN cells. Whole cell patch clamp recordings were conducted on 9-17 day old rat brainstem slices in the presence of the synaptic blockers gabazine (GABAA antagonist), strychnine (glycine antagonist), 6-cyano-7-nitroquinoxaline-2,3-dione (AMPA/kainate receptor antagonist), and APV (NMDA receptor antagonist) for Ih experiments; synaptic blockers plus tetrathylammonium chloride (to block K+ channels), cadmium and nickel chloride (to block Ca channels) were used in the Na+ current experiments. SLAN-4 reduced the blockade of INa (~50%) and IH (~93%) caused by leptin. Intracellular GDPbeta[a G-protein inhibitor] significantly blocked the effect of leptin on INa (~60%) but not on IH (~25%). Intracellular GTPgamma (a G-protein activator) blocked the effect of leptin on both INa (~80%) and IH (~90%). These results suggest that these effects of leptin are G-protein dependent and can be blocked by SLAN-4. We also found that leptin enhanced NMDA receptor-mediated responses in the PPN population as a whole, an effect blocked by SLAN-4. These results show that leptin’s effect on PPN cells is not only G-protein dependent, but also receptor mediated. We hypothesize that leptin normally decreases activity in the PPN by reducing IH and INa currents, and that in obesity, this effect may be blunted due to leptin resistance, leading to increased arousals and REM sleep drive.
NS54 Effects of ApoE, Reelin, and IL-4 on Mitochondrial Respiratory Gene Expression as a Model for the Neuropathology of Alzheimer

Jenny Koo
Undergraduate Student, University of Arkansas, Fayetteville
hkoo@uark.edu

Recent studies have independently suggested critical roles for neuroinflammation and altered mitochondrial metabolism in the neuropathology of Alzheimer’s disease (AD), but it is not clear whether these two phenomena are linked. Apolipoprotein E4 (ApoE4) is a known genetic risk factor for late-onset of AD, with the ε4 allele being associated with much higher rates of the disease than seen with the more common ε3 allele. As a key factor in the shuttling of lipids between tissues and cells, ApoE has been speculated to influence cellular metabolism, and ApoE genotype can significantly impact neuroinflammation. The extracellular matrix glycoprotein Reelin binds some of the same receptors as ApoE and thus may have some of the same effects. Interleukin-4 (IL-4) has been touted as a potential therapeutic agent as it can dramatically alter the behavior of inflammatory mediators, particularly microglia. The products of the ε3 and ε4 alleles of ApoE (ApoE3 and ApoE4, respectively), Reelin, IL-4 and combinations of these were tested on rat primary astrocyte and microglial cultures for effects on the expression of mitochondrial enzymes NADH dehydrogenase ubiquinone beta subcomplex 8 (Ndufb8), oxoglutarate dehydrogenase (Ogdh), ubiquinol cytochrome c reductase core protein 2 (Uqcrcc2), and translocator protein (Tspo). Quantitative RT-PCR (qRT-PCR) was used to assess gene expression of the mitochondrial enzymes. Preliminary indications show that there is a significant increase in Ogdh resulting from ApoE4, whereas previous studies found that AD is associated with a decrease in the enzyme activity to which Ogdh contributes. Though surprising, these results may be explained by additional ongoing experiments.

NS55 Determining the Role of Neurogenin1 in the Development of the Mouse Dorsal Root Ganglion

Stephen A. Shrum
Undergraduate Student, Hendrix College
shrumsa@hendrix.edu

Neurogenin1 (ngn1) is a transcription factor that is required for the development of one subtype of neuron in the dorsal root ganglion (DRG) since ngn1 knockout mice specifically lack pain-sensing nociceptive neurons. The lack of one differentiated neural cell type could be the result of a defect in differentiation of that particular cell type or a defect in neural vs. glial fate determination in an uncommitted progenitor. Because an analogous gene in the olfactory system (mash1) plays a role in neural vs. glial fate determination in that tissue, we hypothesize that ngn1 functions in neural vs. glial fate determination in the DRG. To test this hypothesis, we will compare the expression of known cell-type specific markers to determine the developmental fate of cells in the absence of ngn1 function in ngn1 knockout embryos. If ngn1 is involved in neural fate determination we would expect a decrease in the proportion of nociceptors and an increase in the proportion of glial cells in knockout mice relative to their wild-type littermates. Mice heterozygous for the ngn1 knockout allele were bred to produce wild-type and knockout embryos. The expression of cell-type specific markers was analyzed on transverse tissue sections from embryonic day (E) 10-12.5 as this time encompasses the onset of ngn1 expression and the peak of DRG neurogenesis. We performed in situ hybridization with cell-type specific probes to detect neural crest progenitor cells, sensory neuron subtypes, and glial cells. Our current data is consistent with ngn1 functioning in neural fate determination as we have observed a decrease in nociceptors and an increase in the proportion of glial cells in the DRG of ngn1 knockout mice. Supported by the Summer Mentored Faculty Fellowship Program of the Arkansas INBRE (P20 RR 16460).
NS56  Conditional Lineage Tracing in the Mouse Dorsal Root Ganglion

Kaleb H. Wolfe
Undergraduate Student, Hendrix College
wolfekh@hendrix.edu

Kaleb H. Wolfe, Richard C. Murray, Hendrix College

Chronic pain, often a result of damage to neurons in the dorsal root ganglia (DRG), is one of the most widespread diseases in the United States. A better understanding of the development of DRG neurons could help produce new treatments for this condition. During early development, DRG neurons begin as neural crest cells which first differentiate into neural or glial progenitors (neural fate determination). The progenitors then further develop into specific neural or glial subtypes. Previous research has found that the transcription factor neurogenin1 (ngn1) is critical in the development of the nociceptive neuron subtype. Based on this and other work from the lab, we hypothesize that ngn1 plays a role in neural fate determination in the DRG. If this hypothesis is correct, ngn1 may be expressed by neural crest cells and subsequently maintained by neural progenitors and down-regulated in glial progenitors. To test this prediction, we conditionally labeled ngn1-expressing cells during DRG development to follow their cell fate. Conditional labeling required the use of the offspring of two transgenic mouse lines. One of these lines expresses a conditional cre recombinase enzyme (creER) under the control of ngn1 promoter sequences, and the other expresses a ubiquitous lacZ reporter gene inactivated by a translational stop. The translational stop can be removed in cells expressing the creER protein by injecting tamoxifen into the animal. Pregnant females were injected with tamoxifen at E11.5 (the peak of neurogenesis in the DRG). At E12.5, E16.5 and P21, sections of the DRG were labeled for the reporter gene as well as glial or neural markers in order to discover the identity of the progeny of the ngn1-expressing cells. We have identified neurons derived from ngn1-expressing progenitors and are currently looking for evidence of labeled glial cells. Supported by the Summer Mentored Faculty Fellowship Program of the Arkansas INBRE (P20 RR 16460).

NS57  Characterization of Active Transporter Systems at Blood-Brain Barrier

Kelin Key
Undergraduate Student, University of Arkansas at Pine Bluff
ricea@uapb.edu

Kelin Key, Kameron Lee, Trenton Ware, and Antonie H. Rice, Ph.D.. University of Arkansas at Pine Bluff

The delivery of therapeutic drugs to the brain continues to be a challenge for the pharmaceutical industry. The blood-brain barrier (BBB) regulates the influx and efflux of a wide variety of substances, and remains the major obstacle in the delivery of drugs to the central nervous system (CNS). Various strategies have been devised to circumvent the BBB in order to increase drug delivery to CNS. The purpose of this work was to assess the potential mechanistic pathways present at the Blood-brain barrier in bovine microvessel endothelial cells (BBMECs). The following transporters were characterized in the BBMEC cell culture system: a) the monocarboxylic acid transporter (MCT), and b) the organic anion transporter (OAT). Western blot analysis was employed to demonstrate the presence of each transporter. These transporters were characterized by assessing the uptake and permeability properties of known substrates. To assess the functionality of each transporter, uptake experiments were performed in the presence/absence of known metabolic inhibitors of the transporters. Competitive uptake and permeability experiments were also performed for each. The experiments demonstrate that all of the transporters are present and actively functional in the BBMEC system. These transporters offer alternate routes for delivering therapeutics to the brain that may exhibit poor brain/CNS bioavailability.
The delivery of therapeutic drugs to the brain continues to be a challenge for the pharmaceutical industry. The blood-brain barrier (BBB) regulates the influx and efflux of a wide variety of substances, and remains the major obstacle in the delivery of drugs to the central nervous system (CNS). Various strategies have been devised to circumvent the BBB in order to increase drug delivery to CNS. The purpose of this work was to assess the potential mechanistic pathways present at the Blood-brain barrier in bovine microvessel endothelial cells (BBMECs) and to demonstrate that active transporters exist at the BBB that may provide alternative routes for delivering therapeutics to the brain that may exhibit poor brain/CNS bioavailability, and to also assess the potential mechanistic pathway of a newly synthesized taxane, TX-67, across the BBB. Previously, we demonstrated the functionality of the following transporters in the BBMEC cell culture system: a) the monocarboxylic acid transporter (MCT), and b) the organic anion transporter (OAT). The following work demonstrates the presence and activity of Na+ dependent dicarboxylate transporter (NaDC) in BBMEC cell culture system. To characterize the functionality of the NaDC transporter, typical substrates were selected to perform uptake and transport experiments. The NaDC substrates selected were succinate, glutarate, fumarate, α-ketoglutarate, and maleate. Competitive inhibitions studies using each of the substrates and Taxane analogue Tx-67 were also performed. The results demonstrate that the transporter is present and functional in BBMECs. The data also suggest that the enhanced permeation of Tx-67 may be explained by the utilization of the NaDC transporter at the BBB.

No amount of experimentation can ever prove me right; a single experiment can prove me wrong.

Albert Einstein
Sponsor Acknowledgements

National Institutes of Health (NIH)

National Institute of General Medical Sciences (NIGMS)

Institutional Development Award Program (IDeA)

Arkansas IDeA Networks of Biomedical Research Excellence (AR INBRE) – P20GM103429

Arkansas Center for Microbial Pathogenesis and Host Inflammatory Responses (COBRE) – P20GM103625

Arkansas Center for Translational Neuroscience (COBRE) P20GM103425

Arkansas Center for Protein Structure and Function (COBRE) P20GM103450

University of Arkansas for Medical Sciences (UAMS)

Nikon

Denville Scientific Inc.

Riceland Foods, Inc.

Cavender’s All Purpose Greek Seasoning
<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>University/Affiliation</th>
<th>Email</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adelmund, Steven</td>
<td>Graduate Research Assistant</td>
<td>Louisiana State University - Shreveport</td>
<td><a href="mailto:tgilbert@lsu.edu">tgilbert@lsu.edu</a></td>
</tr>
<tr>
<td>Ahmed, Sara</td>
<td>Director of Sequencing</td>
<td>Cofactor Genomics</td>
<td><a href="mailto:sara_ahmed@cofactorgenomics.com">sara_ahmed@cofactorgenomics.com</a></td>
</tr>
<tr>
<td>Akhter, Noor</td>
<td>Assistant Professor</td>
<td>University of Arkansas for Medical Sciences</td>
<td><a href="mailto:lusterlindad@uams.edu">lusterlindad@uams.edu</a></td>
</tr>
<tr>
<td>Allensworth-James, Melody</td>
<td>Graduate Assistant</td>
<td>University of Arkansas for Medical Sciences</td>
<td><a href="mailto:mallensworth@uams.edu">mallensworth@uams.edu</a></td>
</tr>
<tr>
<td>Arthur, Christine</td>
<td>Student</td>
<td>University of Arkansas for Medical Sciences</td>
<td><a href="mailto:mcarthur2@uams.edu">mcarthur2@uams.edu</a></td>
</tr>
<tr>
<td>Balasubramaniam, Meenakshisundaram</td>
<td>Graduate student in Bioinformatics</td>
<td>UAMS / UALR</td>
<td><a href="mailto:sundaram.m87@gmail.com">sundaram.m87@gmail.com</a></td>
</tr>
<tr>
<td>Barber, Eric</td>
<td>Graduate Student</td>
<td>University of Arkansas</td>
<td><a href="mailto:edbarber@email.uark.edu">edbarber@email.uark.edu</a></td>
</tr>
<tr>
<td>Barth, Jeremy</td>
<td>Assistant Professor</td>
<td>Medical University of South Carolina</td>
<td><a href="mailto:barthj@musc.edu">barthj@musc.edu</a></td>
</tr>
<tr>
<td>Batarseh, Yazan</td>
<td>Graduate Student</td>
<td>University of Louisiana at Monroe</td>
<td><a href="mailto:tgilbert@lsu.edu">tgilbert@lsu.edu</a></td>
</tr>
<tr>
<td>Batra, Sanjay</td>
<td>Assistant Professor-Research</td>
<td>Louisiana State University</td>
<td><a href="mailto:sbatra@lsu.edu">sbatra@lsu.edu</a></td>
</tr>
<tr>
<td>Batte, Justin</td>
<td>Graduate Student</td>
<td>The University of Southern Mississippi</td>
<td><a href="mailto:justin.batte@eagles.usm.edu">justin.batte@eagles.usm.edu</a></td>
</tr>
<tr>
<td>Bauer, Michael</td>
<td>Post Doctoral Fellow</td>
<td>University of Arkansas for Medical Sciences</td>
<td><a href="mailto:mbauer2@uams.edu">mbauer2@uams.edu</a></td>
</tr>
<tr>
<td>Beck, Paige</td>
<td>Center For Translational Neuroscience</td>
<td>University of Arkansas for Medical Sciences</td>
<td><a href="mailto:pbbeck@uams.edu">pbbeck@uams.edu</a></td>
</tr>
<tr>
<td>Beneš, Helen</td>
<td>Professor &amp; Associate Director AR INBRE</td>
<td>University of Arkansas for Medical Sciences</td>
<td><a href="mailto:beneshelen@uams.edu">beneshelen@uams.edu</a></td>
</tr>
<tr>
<td>Berbuuse, Greg</td>
<td>graduate student</td>
<td>University of Central Arkansas</td>
<td><a href="mailto:gberbusse@gmail.com">gberbusse@gmail.com</a></td>
</tr>
<tr>
<td>Bishop, Sarah</td>
<td>Undergraduate Student</td>
<td>Ouachita Baptist University</td>
<td><a href="mailto:bis48801@obu.edu">bis48801@obu.edu</a></td>
</tr>
<tr>
<td>Blair, William</td>
<td>Undergraduate Researcher</td>
<td>Arkansas State University</td>
<td><a href="mailto:william.blair@smail.astate.edu">william.blair@smail.astate.edu</a></td>
</tr>
<tr>
<td>Blanchett, Logan</td>
<td>Graduate Student</td>
<td>The University of Southern Mississippi</td>
<td><a href="mailto:logan.blancett@usm.edu">logan.blancett@usm.edu</a></td>
</tr>
<tr>
<td>Blevins, Jon</td>
<td>Assistant Professor</td>
<td>University of Arkansas for Medical Sciences Dept. of Microbiology and Immunology</td>
<td><a href="mailto:jsblevins@uams.edu">jsblevins@uams.edu</a></td>
</tr>
<tr>
<td>Boehme, Karl</td>
<td>Assistant Professor</td>
<td>University of Arkansas for Medical Sciences</td>
<td><a href="mailto:kwboehme@uams.edu">kwboehme@uams.edu</a></td>
</tr>
<tr>
<td>Bow, Eric</td>
<td>Graduate Student</td>
<td>University of Mississippi</td>
<td><a href="mailto:ebow@go.olemiss.edu">ebow@go.olemiss.edu</a></td>
</tr>
<tr>
<td>Brochhausen, Mathias</td>
<td>Assistant Professor</td>
<td>University of Arkansas for Medical Sciences</td>
<td><a href="mailto:mbrochhausen@uams.edu">mbrochhausen@uams.edu</a></td>
</tr>
<tr>
<td>Brown, Aliza T</td>
<td>Assistant Professor</td>
<td>University of Arkansas for Medical Sciences</td>
<td><a href="mailto:atbrown@uams.edu">atbrown@uams.edu</a></td>
</tr>
<tr>
<td>Brown, LaRae</td>
<td>Graduate Student</td>
<td>University of Arkansas</td>
<td><a href="mailto:ldb002@uark.edu">ldb002@uark.edu</a></td>
</tr>
<tr>
<td>Burks, Jared</td>
<td>Student</td>
<td>Arkansas State University</td>
<td><a href="mailto:Jared.Burks@mail.astate.edu">Jared.Burks@mail.astate.edu</a></td>
</tr>
<tr>
<td>Burroughs, Mallory</td>
<td>Student</td>
<td>Ouachita Baptist University</td>
<td><a href="mailto:bur51519@obu.edu">bur51519@obu.edu</a></td>
</tr>
<tr>
<td>Butler, Khatiana</td>
<td>Student</td>
<td>University of Arkansas At Pine Bluff</td>
<td><a href="mailto:butlerk@uapb.edu">butlerk@uapb.edu</a></td>
</tr>
<tr>
<td>Byrum, Stephanie</td>
<td>Instructor</td>
<td>University of Arkansas for Medical Sciences</td>
<td><a href="mailto:sbyrum@uams.edu">sbyrum@uams.edu</a></td>
</tr>
<tr>
<td>Caro, Andres</td>
<td>Chemistry Department, Hendrix College</td>
<td></td>
<td><a href="mailto:caro@hendrix.edu">caro@hendrix.edu</a></td>
</tr>
<tr>
<td>Carr, Sarah</td>
<td>Student</td>
<td>Ouachita Baptist University</td>
<td><a href="mailto:car49989@obu.edu">car49989@obu.edu</a></td>
</tr>
<tr>
<td>Castillo, Sonia</td>
<td>Graduate Student</td>
<td>Arkansas State University</td>
<td><a href="mailto:sonia.castillo@mail.astate.edu">sonia.castillo@mail.astate.edu</a></td>
</tr>
<tr>
<td>Chancellor, Shana</td>
<td>Student</td>
<td>University of Arkansas at Monticello</td>
<td><a href="mailto:smc04845@uamont.edu">smc04845@uamont.edu</a></td>
</tr>
<tr>
<td>Chavan, Shweta</td>
<td>Post Doctoral Fellow, UAMS</td>
<td></td>
<td><a href="mailto:schavan@uams.edu">schavan@uams.edu</a></td>
</tr>
</tbody>
</table>
Chen, Jing  
Arkansas State University  
jchen@astate.edu

Childs, Gwen  
Professor and Chair  
University of Arkansas for Medical Sciences  
childsgwen@uams.edu

Cleavenger, Jordyn  
Student, University of Central Arkansas  
jcleavenger1@uca.edu

Cook, Cody, M.D., Ph.D.  
Graduate Assistant, UAMS  
Cookcody@uams.edu

Cooper, Nigel  
Professor, University of Louisville  
nigelcooper@louisville.edu

Cornett, Larry  
Vice Chancellor for Research & Director AR INBRE  
University of Arkansas for Medical Sciences  
cornettlawrencee@uams.edu

Crabtree, Nathan  
Graduate Student, UALR/UAMS  
nmcrabtree@ualr.edu

Cramer, Carole  
Professor, Arkansas State University  
ccramer@astate.edu

Crossley, Davida  
Post Doctoral Researcher  
Alcorn State University  
dcrossley@alcorn.edu

Currey, Dorothy  
Summer Science Student, UAMS/COBRE  
dcurrey@email.uark.edu

Cutler, Stephen  
Chair and Professor  
University of Mississippi  
cutler@olemiss.edu

Davis, Cheryl  
Professor, Western Kentucky University  
cheryl.davis@wku.edu

Dearolf, Jennifer  
Associate Professor, Hendrix College  
dearolf@hendrix.edu

Deininger, Prescott  
Director Tulane Cancer Center  
Tulane University  
pdeinin@tulane.edu

Denefe, Matt  
Student, University of Central Arkansas  
mddenefel@gmail.edu

Desai, Aesha  
Graduate Student, Clemson University  
adesai@clemson.edu

DeYoung, Luke  
Student, John Brown University  
DeYoungL@jbu.edu

Dhamad, Ahmed  
Graduate Student, University of Arkansas  
adhamad@uark.edu

Dillon, Glenn  
VP for Health Sciences Research & Graduate Education  
West Virginia University  
tluci@hsc.wvu.edu

Doerksen, Robert  
Associate Professor  
University of Mississippi  
rjd@olemiss.edu

D’Onofrio, Stasia  
Center for Translational Neuroscience  
University of Arkansas for Medical Sciences  
smdonofrio@uams.edu

Dunlap, Hope  
Student, University of Arkansas Monticello  
hiv0405@uamont.edu

Durand, Kirt  
Graduate Student, Purdue University  
kdurand@ purdue.edu

Durdik, Jeannine  
Associate Dean  
University of Arkansas Fayetteville  
jdurdik@uark.edu

Ejiofor, Shannon  
Chemistry Department, Hendrix College  
atressa2000@yahoo.com

Elasri, Mohamed  
Professor  
University of Southern Mississippi  
mohamed.elasri@usm.edu

Eldridge, Jacqueline  
Student, INBRE Scholar’s Program  
jacqueline_13e@yahoo.com

ElSohly, Mahmoud  
Research Professor, University of MS  
melsohly@olemiss.edu

Embers, Monica  
Research Assistant Professor  
Tulane National Primate Research Center  
members@tulane.edu

Eoff, Robert  
Assistant Professor  
University of Arkansas for Medical Sciences  
rleoff@uams.edu

Estrada, John  
Associate Professor  
LSUHSC - Cancer Center  
jesta@lsuhsc.edu

Fahim, Arjang  
Graduate Student  
University of South Carolina  
fahim@email.sc.edu

FanteGrossi, William  
Assistant Professor  
University of Arkansas for Medical Sciences  
wefontegrossi@uams.edu

Fleming, James  
Graduate Student  
University of Central Arkansas  
jdaniel.fleming@gmail.com

Fondufe-Mittendorf, Yvonne  
Professor, University of Kentucky  
y.fondufe-mittendorf@uky.edu

Foster, Timothy  
Associate Professor  
LSUHSC - Cancer Center and MIP  
tfoste@lsuhsc.edu

Funk, Joel  
Assistant professor  
John Brown University  
jofunk@jbu.edu

Galperin, Emilia  
Assistant Professor, University of Kentucky  
emilia.galperin@uky.edu

Gannon, Brenda  
Graduate Student  
University of Arkansas for Medical Sciences  
bagannon@uams.edu

Gao, Feng  
Post Doctoral Fellow, University of Arkansas  
fg003@uark.edu

Garcia-Rill, Edgar  
Director, UAMS Center for Translational Neuroscience  
garciarilledgar@uams.edu
Garrison, Kevin  
Associate Professor  
University of Central Arkansas  
kgarrison@uca.edu

Gemene, Kebede  
Assistant professor  
Northern Kentucky University  
gemenek1@nku.edu

Gettys, Thomas  
Professor  
Pennington Biomedical Research Center  
cindi.tramonte@pbrc.edu

Ghai, Pooja  
Student  
Arkansas State University  
pooja.ghai@smail.astate.edu

Ghosh, Debopam  
Graduate Student  
University of Arkansas for Medical Sciences  
dgosh@uams.edu

Gibson, Justin  
Undergraduate Student  
Northern Kentucky University  
gibsonj11@mymail.nku.edu

Gibson, Laura  
Deputy Director, WVU MBRCC  
lgibson@hsc.wvu.edu

Gill, Nicholas  
Student, Hendrix College  
GillNP@hendrix.edu

Glazko, Galina  
Assistant Professor  
University of Arkansas for Medical Sciences  
gvglazko@uams.edu

Gokhale, Ameya  
Graduate Student  
University of Louisiana at Monroe  
tgilbert@lsu.edu

Govindarajan, Mugunthan  
Research Associate, University of Arkansas  
mgovinda@uark.edu

Gray, Raven  
Student, Inbre Scholar’s Program  
r.gray1291@gmail.com

Gray, Wayne  
Professor  
University of Arkansas for Medical Sciences  
grgrayanel@uams.edu

Greathouse, Denise  
Research Associate Professor  
University of Arkansas  
dgreatho@uark.edu

Greene, Jennifer  
Undergraduate Research Assistant  
University of Charleston  
greenej0221@gmail.com

Greer-Williams, Nancy  
Assistant Professor  
University of Arkansas for Medical Sciences  
irelandtracim@uams.edu

Guerrero-Plata, Antonieta  
Assistant Professor  
Louisiana State University  
aguerrp@lsu.edu

Guo, Zibiao  
Research Scientist  
University of Mississippi Medical Center  
zguo@umc.edu

Hall, M.D., Richard  
Professor  
University of Arkansas for Medical Sciences  
hallrichardw@uams.edu

Hardy, Drake  
Student, Ouachita Baptist University  
har50046@obu.edu

Hauer-Jensen, Martin  
Professor  
University of Arkansas for Medical Sciences  
mhjensen@life.uams.edu

Hayar, Abdallah  
Associate Professor, UAMS  
amhayar@uams.edu

Henderson, Ashley  
Graduate Student, University of Arkansas  
amartfel@email.uark.edu

Hendrickson, Howard  
Associate Professor  
University of Arkansas for Medical Sciences  
hendricksonhowardp@uams.edu

Hensley, Lori  
Chair, Department of Biology  
Ouachita Baptist University  
hensleyl@obu.edu

Hill, Brent  
Associate Professor  
University of Central Arkansas  
bhill@uca.edu

Hoehn, James  
Executive Director EPSCoR/IDeA Foundation  
jhoehn@epscorfoundation.org

Hofmann, Emily  
Student, Northern Kentucky University  
hofmanne1@mymail.nku.edu

Hogan, William  
Professor  
University of Arkansas for Medical Sciences  
wrhogan@uams.edu

Horton, Tim  
Student, Ouachita Baptist University  
hor46650@obu.edu

House, Taylor  
Medical Student  
University of Arkansas for Medical Sciences  
xhuang@astate.edu

Houser, Anne  
Program Analyst, OLPA/OD/NIH  
vot@mail.nih.gov

Howard, Lacey  
Graduate Student  
University of Southern Mississippi  
laceyrlhoward@yahoo.com

Huang, Xiuzhen  
Associate Professor  
Arkansas State University  
xhuang@astate.edu

Hyatt, William  
Research Technician  
University of Arkansas for Medical Sciences  
wshyatt@uams.edu

Hyde, James  
Center for Translational Neuroscience  
University of Arkansas for Medical Sciences  
jrhyde@uams.edu

Jaiswal, Mihir  
Graduate Student, UALR/UAMS  
msjaiswal@ualr.edu

James, Andrew  
Assistant Professor, U of A Medical Sciences  
gajames@uams.edu

Jeffers, Joe  
Professor, Ouachita Baptist University  
jjeffers@obu.edu

Johann, Donald  
Associate Professor, UAMS  
djohann@uams.edu
Johnson, Wayne  
Board Member  
Science & Technology Research in America

Jones, Drew  
Postdoctoral Research Associate  
St Jude Children’s Research Hospital  
DrewRJones@Gmail.com

Jovin, Cindy  
Undergraduate Student  
University of Central Arkansas  
gcupid@ymail.com

Kaddoumi, Amal  
Associate professor  
University of Louisiana at Monroe  
kaddoumi@ulm.edu

Kane, Cynthia  
Professor  
University of Arkansas for Medical Sciences  
kanecynthia@uams.edu

Kapusta, Daniel  
Professor and COBRE PI/Director  
LSU Health Sciences Center - New Orleans  
dkapus@lsuhsc.edu

Kaushal, Gagan  
Associate Professor  
Thomas Jefferson University  
gagan.kausal@jefferson.edu

Kelley, Melissa  
Associate Professor  
University of Central Arkansas  
choffman@uca.edu

Kezunovic, Nebojsa  
Center for Translational Neuroscience  
University of Arkansas for Medical Sciences  
nkezunovic@uams.edu

Kiaei, Mahmoud  
Assistant Professor  
University of Arkansas for Medical Sciences  
mkiaei@uams.edu

King, Rodney  
Professor, Western Kentucky University  
rodney.king@wku.edu

Kiseleva, Raisa  
Graduate Student, Clemson University  
rkisele@g.clemson.edu

Klei, Thomas  
Professor  
School of Veterinary Medicine, LSU  
tgilbert@lsu.edu

Koeppe, Roger  
Professor, University of Arkansas  
rk2@uark.edu

Kompelli, Anvesh  
Student, Hendrix College  
kompelli@hendrix.edu

Koo, Jenny  
Student, Arkansas INBRE  
hkoo@uark.edu

Kousoulas, Konstantin  
Professor, Louisiana State University  
vguk@lsu.edu

Kumar, Ajay  
Assistant Professor  
Universidad Metropolitana  
um_gcora@suagm.edu

LaFranzo, Natalie  
Project Scientist, Cofactor Genomics  
natalie_lafrazo@cofactorgenomics.com

Lairamore, PhD, PT, Chad  
Assistant Professor  
University of Central Arkansas  
chadl@uca.edu

Lawrence, Mark  
Professor D.V.M.  
Mississippi State University  
lawrence@cvm.msstate.edu

Layton, Lachan  
Undergraduate Student  
University of Central Arkansas  
lachanlayton@gmail.com

Lee, Kameron  
Student, University of Arkansas At Pine Bluff  
ricea@uapb.edu

Lin, Xiong  
Post Doctoral Fellow  
University of Arkansas for Medical Sciences  
xblin@uams.edu

Lindsey, Miki  
Undergraduate Student  
University of Central Arkansas  
mlindsey2@uca.edu

Little, Scott  
Director, SC EPSCoR/IDeA  
slittle@mailbox.sc.edu

Liu, Jia  
Assistant Professor  
University of Arkansas for Medical Sciences  
jliu4@uams.edu

Lorence, Argelia  
Associate Professor in Metabolic Engineering  
Arkansas State University  
alorence@astate.edu

Lorsch, Jon R.  
NIGMS Director  
National Institutes of Health  
jon.lorsch@nih.gov

Luo, Heng  
Graduate Student  
University of Arkansas at Little Rock  
xluo@ualr.edu

Luster, Brennon  
Center for Translational Neuroscience  
University of Arkansas for Medical Sciences  
bluster@uams.edu

Mack, Franshawn  
Undergraduate Student  
South Carolina State University  
fmack20@scsu.edu

MacNicol, Angus  
Professor  
University of Arkansas for Medical Sciences  
mnicol@UAMS.edu

MacNicol, Melanie  
Assistant Professor, UAMS/CTN  
mnicol@UAMS.edu

Mancino, Michael  
Associate Professor  
University of Arkansas for Medical Sciences  
mjmanino@uams.edu

Markwald, Roger  
Professor  
MUSC-Regenerative Medicine & Cell Biology  
markwald@musc.edu
Marquis, Bryce  
Professor, University of Central Arkansas  
choffman@uca.edu

Marshall, Ramey  
Medical Student  
University of Arkansas for Medical Sciences  
rmarshall@uams.edu

Martin, Karen  
Director, Imaging Facilities  
West Virginia University  
kamartin@hsc.wvu.edu

Martinez, Osmarie  
Graduate Student  
Univ de Puerto Rico Recinto de Ciencias Médicas  
Osmarie.martinez@upr.edu

Martinez-Ceballos, Eduardo  
Associate Professor  
Southern University  
Louisianaeduardo_martinez@subr.edu

Martinez-Montemayor, Michelle M  
Assistant Professor  
Universidad Central Del Caribe  
abaez@uccaribe.edu

Mattingly, Bruce  
Program Coordinator, Kentucky INBRE  
b.mattin@morehead-st.edu

McClure, Gail  
Program Director  
Arkansas Science & Technology Authority  
gail.mcclure@arkansas.gov

McGehee, Nicole  
Student, INBRE Scholar's Program  
mcgehee.nicole@gmail.com

McNeill, Tyana  
Student, South Carolina State University  
tmcneill@scsu.edu

Mennemeier, Mark  
Professor  
University of Arkansas for Medical Sciences  
Neurobiology and Dev. Scs  
msmennemeier@uams.edu

Messias, Erica  
Associate Professor  
University of Arkansas for Medical Sciences  
emessias@uams.edu

Meyer, Jessie  
Student, Ouachita Baptist University  
mey51199@obu.edu

Milam, Addie  
Student, University of Central Arkansas  
amilam1@uca.edu

Millett, Frank  
Professor, University of Arkansas  
millett@uark.edu

Mitchell, Anita  
Associate Professor  
University of Arkansas for Medical Sciences Center for Translational Neuroscience  
amitchell@uams.edu

Mohamed, Loqman  
Graduate Student  
University of Louisiana at Monroe  
tgilbert@lsu.edu

Montgomery, M.D., James  
Resident  
University of Arkansas for Medical Sciences  
jamesyeye5@yahoo.com

Morrison, Richard  
Professor and Chair  
University of Arkansas for Medical Sciences  
rpmorrison@uams.edu

Moufarrej, Youmna  
Student, Hendrix College  
MoufarrejYE@hendrix.edu

Moussa, Mohamed  
Undergraduate Student  
University of Central Arkansas  
9tanel@gmail.com

Mukiza, Tresor  
Laboratory Technician  
University of Arkansas for Medical Sciences  
TMukiza@uams.edu

Mulkey, Sarah  
Assistant Professor  
University of Arkansas for Medical Sciences  
mulkeysarah@uams.edu

Murphy, E. Angela  
Assistant Professor  
University of South Carolina  
angela.murphy@uscmed.sc.edu

Murray, Richard  
Associate Professor, Hendrix College  
murrayr@hendrix.edu

Nagarkatti, Mitzi  
Carolina Distinguished Professor, Chair  
University of South Carolina  
mitzi.nagarkatti@uscmed.sc.edu

Nagarkatti, Prakash  
VP for Research  
University of South Carolina  
prakash@mailbox.sc.edu

Nabothula, Narasimha  
Research Associate, University of Kentucky  
nna226@uky.edu

Navar, L. Gabriel  
Professor and Chair, Tulane University  
navar@tulane.edu

Naylor, Kari  
Assistant professor  
University of Central Arkansas  
kknaylor@uca.edu

Ni, Amy  
Student, Western Kentucky University  
yan.ni890@topper.wku.edu

Niyonsaba, Edouard  
Undergraduate Student  
University of Central Arkansas  
eniyonsaba1@uca.edu

Norwood, Andrew  
Graduate Student  
University of Arkansas for Medical Sciences  
apnorwood@uams.edu

Nserek可能出现的错误，Aloys  
Student, University of Central Arkansas  
ansereko1@uca.edu

Odle, Angela  
Graduate Student  
University of Arkansas for Medical Sciences  
akodie@uams.edu

Ontko, Allyn  
Associate Professor  
Arkansas State University  
aontko@astate.edu

Otero, Miguel  
Assistant Professor  
University of Puerto Rico-Medical Sciences Campus  
miguel.oter02@upr.edu

Palyok, Phillip  
Undergraduate Student  
Louisiana State University - Shreveport  
rtgilbert@lsu.edu

Pandey, Pankaj  
Graduate Student, University of Mississippi  
pandey@go.olemiss.edu
Paula, Stefan  
Associate Professor  
Northern Kentucky University  
paulas1@nku.edu

Perry, Marty  
Professor, Ouachita Baptist University  
perrym@obu.edu

Peterson, Erich  
Post Doctoral Fellow  
University of Arkansas for Medical Sciences  
eapeterson@uams.edu

Phillips, Matthew  
Graduate Student  
University of Arkansas for Medical Sciences  
mbphillips@uams.edu

Piao, Boyang  
Undergraduate Student  
Louisiana State University  
bpiao1@tigers.lsu.edu

Pirisi-Creek, Lucia  
Principal Investigator/Faculty  
University of South Carolina  
luciapirisicreek@gmail.com

Pollock, Daniel  
Systems Analyst  
University of Arkansas for Medical Sciences  
dlpollock@uams.edu

Pouncey, Dakota  
Student, Hendrix College  
Pounceydl@gmail.com

Powell, Justin  
Resident  
University of Arkansas for Medical Sciences  
justap77@gmail.com

Preston, Kyle  
Student, University of Central Arkansas  
choffman@uca.edu

Prieto, Minolfa  
Assistant Professor  
Tulane University, School of Medicine  
mprieto@tulane.edu

Qosa, Hisham  
Graduate Student  
University of Louisiana at Monroe  
tgilbert@lsu.edu

Rachal, Peyton  
Undergraduate Student  
Louisiana State University - Shreveport  
tgilbert@lsu.edu

Rajagopalan, Venkatesan  
Graduate Student, University of Arkansas  
vxr004@email.uark.edu

Ramirez, Maite  
Doctoral Student  
University of Puerto Rico Medical Sciences  
Campus  
mayte.ramirez@upr.edu

Raney, Kevin  
Professor, Biochemistry & Molecular Biology  
raneykevind@uams.edu

Rankin, Gary  
WV-INBRE PI, Marshall University  
rankin@marshall.edu

Reed, Zach  
Undergraduate Student, Arkansas INBRE  
zgreed@ualr.edu

Reinhard, Danielle  
Graduate Student  
Southern University and A&M  
tgilbert@lsu.edu

Reiss, Robert  
Professor  
University of Arkansas for Medical Sciences / VAMC  
rjsr@uams.edu

Reiss, Krzysztof  
Professor  
LSUHSC - Cancer Center  
kreiss@lsuhsc.edu

Reyna, Nathan  
Associate Professor  
Ouachita Baptist University  
reynan@obu.edu

Rice, Antonie  
Assistant Dean  
University of Arkansas at Pine Bluff  
ricea@uapb.edu

Rimoldi, John  
Professor, University of Mississippi  
jrimoldi@olemiss.edu

Rivera, Carlos  
Student, UPR-RP  
carlos.a.rivera23@gmail.com

Robillard, Katelyn  
Student  
Southeastern Louisiana University  
katelyn.robillard@selu.edu

Robinson, Evan  
Undergraduate student, Clemson University  
ejrobin@g.clemson.edu

Rodriguez, Jorge  
Post Doctoral Fellow  
Clemson University  
jorger@clemson.edu

Rodriguez, Paulo  
Assistant Professor  
LSUHSC - Cancer Center  
PRodri1@lsuhsc.edu

Rodriguez-Medina, Jose  
PR-INBRE PI  
University of Puerto Rico  
jose.rodriguez123@upr.edu

Rouchka, Eric  
Associate Professor  
University of Louisville  
eric.rouchka@louisville.edu

Roy, Kuldeep  
Post Doctoral Fellow  
The University of Mississippi  
kkroy@olemiss.edu

Sagers, Cynthia  
Associate VP Research  
University of Arkansas  
csagers@uark.edu

Saha, Rinku  
Graduate Student, UALR/Bioinformatics  
rxsaha@ualr.edu

Saha, Somdutta  
Graduate Student, UALR/UAMS  
sxsaha@ualr.edu

Sahukhal, Gyan  
Graduate Student  
University of Southern Mississippi  
gyan.sahukhal@eagles.usm.edu

Saied, Ahmad  
Graduate Student  
Louisiana State University  
asaied@lsu.edu

Sakon, Joshua  
Associate Professor, University of Arkansas  
jtsakon@uark.edu

Salinas, Eduardo  
Student  
University of Arkansas for Medical Sciences  
esalinas@uams.edu
Salley, Dr. Judith  
Professor, South Carolina State University  
djdsalley@scsu.edu

Samanta, Dhritiman  
Graduate Student  
The University of Southern Mississippi  
dhritiman.samanta@eagles.usm.edu

Santanam, Nalini  
Professor  
Marshall University School of Medicine  
santanam@marshall.edu

Sato, Akemi  
Lab. Manager, Tulane University  
asato@tulane.edu

Sato, Ryosuke  
Instructor, Tulane University  
rasto@tulane.edu

Satyanarayanajois, Seetharama  
Associate Professor  
University of Louisiana at Monroe  
jois@ulm.edu

Schlagel, Chad  
Student, John Brown University  
schlagelc@jbu.edu

Schrader, Sarah  
Student, Western Kentucky University  
sarah.schrader435@gmail.com

Schurko, Andrew  
Professor, Hendrix College  
schurko@hendrix.edu

Settle, Michelle  
Graduate Student  
University of Central Arkansas  
mlsettle02@gmail.com

Sevilla, Gabby  
Undergraduate Student  
Northern Kentucky University  
sevillag1@mymail.nku.edu

Shaffer, Jacob  
Student, Northern Kentucky University  
shafferj1@mymail.nku.edu

Sharma, Priyanka  
Doctoral Candidate, University of Arkansas  
pxs010@email.uark.edu

Shearer, Glen  
Principal Investigator  
University of Southern Mississippi  
glen.shearer@usm.edu

Shen, Shu  
RA, University of Kentucky  
shu.shen@uky.edu

Shi, Wei  
Assistant Professor, University of Arkansas  
weishi@uark.edu

Shrum, Stephen  
Student, Hendrix College  
shrumsa@hendrix.edu

Sifford, Jeffrey  
Professor  
University of Arkansas for Medical Sciences  
jsifford@uams.edu

Simon, Emily  
Research Assistant  
University of Arkansas for Medical Sciences  
ejsimon@uams.edu

Skinner, Robert  
Professor  
University of Arkansas for Medical Sciences  
rskinner@uams.edu

Smeltzer, Mark  
OBRE Director  
University of Arkansas for Medical Sciences  
smeltzermarks@uams.edu

Smith, Erin  
Honors Student  
University of Southern Mississippi  
e.michelle.smith@eagles.usm.edu

Smith, Michael  
Associate Professor  
Western Kentucky University  
michael.smith1@wku.edu

Soto, Israel  
Undergraduate Student  
Louisiana State University - Shreveport  
tgilbert@lsu.edu

Spirou, George  
Director, Center for Neuroscience  
West Virginia University  
gspirou@hsc.wvu.edu

Srivatsan, Malathi  
Associate Director  
ASU Arkansas Biosciences Institute  
ljeffery@astate.edu

Stahl, James  
Student  
University of Arkansas for Medical Sciences  
jstahl@uams.edu

Stamp-Siegfried, Rachel  
Medical Student  
University of Arkansas for Medical Sciences  
RStampSiegfried@uams.edu

Stanfield, Brent  
Graduate Student  
Louisiana State University  
brentstanfield@gmail.com

Stenken, Julie  
Professor, University of Arkansas  
jstenken@uark.edu

Stewart, Mary  
Associate Professor  
University of Arkansas at Monticello  
stewartm@uamont.edu

Stockmeier, Craig  
Professor  
University of Mississippi Medical Center  
cstockmeier@umc.edu

Stone, Ramona-Elena  
Research Faculty, Health Behavior  
University of Kentucky  
rst229@uky.edu

Stromberg, Arnold  
Chair/Professor, University of Kentucky  
Stromberg@uky.edu

Strome, Erin  
Assistant Professor  
Northern Kentucky University  
strome1@nkue.edu

Strossner, Laura  
Student, Ouachita Baptist University  
str49538@obu.edu

Stuart, Johnasha  
Graduate Student  
University of Arkansas for Medical Sciences  
jdstuart@uams.edu

Stumhofer, Jason  
Assistant Professor  
University of Arkansas for Medical Sciences  
jestumhofer@uams.edu

Suarez-Arroyo, Ivette J  
Graduate Student  
Universidad Central Del Caribe  
abaetz@uccaribe.edu
Sustich, Andy
Vice Provost for Research & Graduate Studies, Arkansas State University
sustich@astate.edu

Syed, Mohsin
Assistant Professor
University of Arkansas for Medical Sciences
lusterlindad@uams.edu

Tackett, Alan
Associate Professor & AR INBRE Core Facility Director, UAMS
AJTackett@uams.edu

Tai, Sherrica
Post Doctoral Fellow
University of Arkansas for Medical Sciences
stai@uams.edu

Taylor, W. Fred
Director, IDeA Program
National Institutes of Health
fred.taylor@nih.gov

Thomas, Kiona
Program Manager
University of South Carolina
scinbre@gmail.com

Tobacyk, Julia
Undergraduate Student
Louisiana Tech University
tgilbert@lsu.edu

Vázquez, Luis
Student, UPR-RP
luigy.vazquez@gmail.com

Vinson, Robert
Assistant Program Manager NIH SBIR/STTR National Institutes of Health
robert.vinson@nih.gov

Von Edwins, Kirby
Comparative Genomics
Ouachita Baptist University
von48723@obu.edu

Voth, Daniel
Assistant Professor
University of Arkansas for Medical Sciences
dvoth@uams.edu

Vyavahare, Naren
Professor, Clemson University
narenv@clemson.edu

Walch, Gretchen
Student, Western Kentucky University
gretchen.walch015@topper.wku.edu

Walker, Ian
Professor, Clemson University
iwalker@clemson.edu

Wang, Hongyuan
Graduate Student
University of Kentucky
hongyuan.wang@uky.edu

Wangila, Grant
Associate Professor
University of Arkansas At Pine Bluff
wangilig@uapb.edu

Warshamana-Greene, Gnana (Saku)
Assistant Professor
South Carolina State University
gwarsham@scsu.edu

Washington, Dominique
Graduate Student
Louisiana State University - Shreveport
tgilbert@lsu.edu

Watts, Alex
Student, University of Central Arkansas
choffman@uca.edu

Weed, Scott
Associate Professor
West Virginia University Mary Babb Randolph Cancer Center
klunsford@hsc.wvu.edu

Wessels, Andy
Professor, MUSC
wesselsa@musc.edu

Williams, Amber
Graduate Student
Louisiana State University - Shreveport
tgilbert@lsu.edu

Williams, Kimerea
Undergraduate Student, LSU Shreveport
tgilbert@lsu.edu

Williams, Philip
Bioinformatics Technical Director
UALR Information Science/Bioinformatics
phwilliams@ualr.edu

Williams, Sara
Student, Ouachita Baptist University
will54475@OBU.EDU

Wischusen, E. William
Associate Professor
Louisiana State University, LBRN Program
tgilbert@lsu.edu

Wolfe, Kaleb
Student, Hendrix College
wolfekh@hendrix.edu

Woods, Laken
Graduate student
University of Central Arkansas
lwoods1@uca.edu

Xiang, Yun
Graduate Student, Clemson University
yxiang@clemson.edu

Xu, Yao
Undergraduate Student
University of Central Arkansas
yxy1@cub.uca.edu

Yactayo-Chang, Jessica
Graduate Student
Arkansas State University
jessica.yactayochang@smail.astate.edu

Yadav, Shilpi
Post Doctoral Fellow
University of Arkansas for Medical Sciences
syadav@uams.edu

Yang, Carrie
Undergraduate Student
Hendrix College
yangcs@hendrix.edu

Yang, Mary
Associate Professor, UALR
mqyang@ualr.edu

Yang, Yuchen
Research Assistant, University of Kentucky
yuchen.y@uky.edu

Yates, Charlie
Associate Professor
University of Central Arkansas & UAMS Center for Translational Neuroscience
cyates@uca.edu

Yu, Shiguang
Assistant Professor
Arkansas State University
syu@astate.edu

Zhang, Haitao
Student, Arkansas State University
haitao.zhang@smail.astate.edu

Zheng, Wenli
Undergraduate Student
Louisiana Tech University
tgilbert@lsu.edu
Zhou, Daohong
Professor
University of Arkansas for Medical Sciences
dzhou@uams.edu

Zhou, Guolei
Assistant Professor
Arkansas State University
gzhou@astate.edu

Zurcher, Grant
Chemistry Department, 
Hendrix College
zurchergf@hendrix.edu

Zymbaylov, Boris
Instructor
University of Arkansas for Medical Sciences
BLZymbaylov@UAMS.edu

The great tragedy of science - the slaying of a beautiful hypothesis by an ugly fact.
Thomas Huxley
Abstract Index

By Thematic Areas

Bioinformatics

BI01 Bauer, Ph.D., Michael, University of Arkansas for Medical Sciences, Leveraging the Old with the New: Integration of Historic Microarray Studies with Next Gen Sequencing for Multiple Myeloma

BI02 Crossley, Ph.D., Davida, Alcorn State University, Characterizing The Function of the M46 Gene In The Pathogenic Fungus Histoplasma capsulatum

BI03 Schrader, Sarah M., Western Kentucky University, Bioinformatic Analysis of Mycobacteriophage TiroTheta9

BI04 McFarland, Devon, University of South Carolina, Utility of mSTALI in Protein Active Site Identification

BI05 Peterson, Ph.D., Erich, University of Arkansas for Medical Sciences, Variant Consensus Reporter: Increasing the Confidence of Variants in Whole Exome Sequencing via a Consensus Approach

BI06 Emby, C. Stephen, University of Arkansas for Medical Sciences/University of Arkansas at Little Rock, NeedleAnalyzer: A Data Analysis Tool for LCMS-Based Untargeted Metabolomics Data

BI07 Fahim, Arjang, University of South Carolina, nDh-PDPA: n-Dimensional Hybrid Probability Density Profile Analysis

BI08 Saha, SoM.D.utta, University of Arkansas for Medical Sciences/University of Arkansas at Little Rock, Defining the Recognition Elements of Lewis Y-Reactive Antibodies

BI09 Robillard, Katelyn, Southeastern Louisiana University, Investigation of the Mechanism of Apparent HPLC Solvent Interference with an Avidin-Binding Assay

BI10 Jaiswal, Mihir, UALR/ UAMS joint bioinformatics graduate program, University of Arkansas at Little Rock, XLPM: X-linked Peptide Mapping Algorithm

BI11 Crabtree, Nathan, University of Arkansas Little Rock and University of Arkansas for Medical Sciences, Adapting a computational evolution system to the analysis of RNA-Seq treatment/response differential gene expression data

BI12 Zybailov, Ph.D., Boris L, University of Arkansas for Medical Sciences, G4 quadruplexes in mitochondrial DNA: a bioinformatics study of their origin, function, and evolution

BI13 Hofmann, Emily, Department of Chemistry, Northern Kentucky University, Identification of novel sarco/endoplasmic reticulum calcium ATPase (SERCA) inhibitors utilizing QSAR modeling

BI14 Glazko, Ph.D., Galina, University of Arkansas for Medical Sciences, Gene Set Net Correlations Analysis (GSNCA): A multivariate differential coexpression test for gene sets

BI15 Walch, Gretchen A., Western Kentucky University, Discovery and Bioinformatic Analysis of Mycobacteriophages Achebe, MooMoo, Simpliphy and Updawg

BI16 Luo, Heng, University of Arkansas at Little Rock, Assessing associations between idiosyncratic reactions-causing drugs and HLA's via computational approaches

BI17 Meyer, Jessie, Ouachita Baptist University, Computational Docking Analysis to Increase Understanding of Chiral Drugs Metabolism

BI18 Burroughs, Mallory, Ouachita Baptist University, Observation of Enantiomeric Specificity in CYP2C9 Using Computational Methods

BI19 Perry, Jr., Ph.D., Martin D., Ouachita Baptist University, Computational docking and analysis of pyrazole derivatives in CYP2E1

BI20 Brochhausen, Ph.D., Mathias, University of Arkansas for Medical Sciences, Extending an ontology for biobank administration to cover data related to studies, study participants and specimens

BI21 Furr, Mercede, University of Arkansas, 3D Structure Model of the Chloroplast Signal Recognition Particle

BI22 Nalabuthula, Ph.D., Narismha, University of Kentucky, Genomic code for Nucleosome positioning is evolutionarily conserved from archaea through man

BI23 Kilgore, Ph.D., Phillip C. S. R., Louisiana State University Shreveport, MotifBrowser: Robust High-Throughput Genome-Wide Mining and Exploration of Motifs

BI24 Saha, Rinku, University of Arkansas for Medical Sciences/University of Arkansas at Little Rock, Computer-aided Drug Design of Inhibitors for Human Cytosolic Malic Enzyme

BI25 Williams, Sara, Ouachita Baptist University, Isolation and Genomic Analysis of Mycobacterium phage RonRayGun

BI26 Shen, Shu, University of Kentucky, An alternative method for analyzing NanoString data

BI27 Rajagopalan, Venkatesan, University of Arkansas, Influence of pH and Side Chain Glutamic Acid on the Behavior of Designed Transmembrane Peptides in Lipid Bilayers

BI28 Hogan, M.D., M.S., William R., University of Arkansas for Medical Sciences, What is information: A representational view and its implications

BI29 Cole, Casey, University of South Carolina, Database of Uca minax transcriptome
Abstract Index

By Thematic Areas

Cancer

CN01 Satyanarayanajois, Ph.D., Seetharama, University of Louisiana at Monroe, EGFR heterodimerization: Dynamics, docking and inhibition of signaling for breast, lung and ovarian cancer

CN02 Grimes, Stuart, Clemson University, Nanoparticle Delivery of Non-Toxic Drugs to Enhance the Efficacy of Chemotherapeutic Drugs

CN03 Phelps, Greg, Arkansas State University, Effects of ionizing Radiation on Guanine Triphosphate Cyclohydrolase 1 Activity

CN04 Hensley, Ph.D., Lori L., Ouachita Baptist University, Antitumor effects of the synthetic cannabinoid aulenic acid on Ewing’s sarcoma

CN05 Johann, Jr., Ph.D., Donald J., University of Arkansas for Medical Sciences, Towards computer assisted laser microdissection

CN06 Rodriguez-Dévora, Jorge I., Clemson University, Miniaturized Bioprinting Platform for Personalized Cancer Therapy

CN07 Weed, Ph.D., Scott A., West Virginia University, Monitoring changes in cervical lymph nodes by high-frequency ultrasound in a 4-NQO mouse model of oral cancer

CN08 Strossner, Laura, Ouachita Baptist University, Creating Model Systems to Study the Effects of Aulenic Acid on Solid Pediatric Tumors

CN09 Chavan, Shweta, University of Arkansas for Medical Sciences, Profiling Multiple Myeloma Engraftment Phenomena via in-vivo SCID Mouse Model and RNA-seq

CN10 Sakon, Ph.D., Joshua, University of Arkansas, Targeting mechanism of prototypical collagen binding domains from clostridial collagenase

CN11 Liu, Ph.D., Jia, Department of Microbiology and Immunology, University of Arkansas for Medical Sciences, Immuno-virotherapy using myxoma virus to treat ovarian cancer

CN12 Murphy, Ph.D., E. Angela, Department of Pathology, Microbiology & Immunology, School of Medicine, University of South Carolina, Quercetin Decreases Tumorigenesis in a Mouse Model of Breast Cancer

CN13 Govindarajan, Mugunthan, University of Arkansas, Fayetteville, Natural glycoconjugate OSW-1 as a tool to discover new therapeutic targets for cancer chemotherapy

CN14 Martin, Ph.D., Karen H, West Virginia University, Imaging Resources for In Vitro and In Vivo Characterization of Cancer-Related Signaling Pathways

CN15 Dhamad, Ahmed E., University of Arkansas, Role of HATx-ERA Complex in ErA-Mediated Transcription in Breast Cancer Cells

CN16 Barletta, Ph.D., Gabriel, University of Puerto Rico - Humacao, Non-toxic and stable nano-carriers for delivering an antitumor agent in vivo

CN17 Ontko, Ph.D., Allyn, Arkansas State University, Effect of Redox Stabilization on Au(II) Anticancer Agents

CN18 Kumar, Ph.D., Ajay, School of Environmental Affairs, Universidad Metropolitana, Structural activity relationship studies of aza-podophyllotoxin derivatives against ovarian human tumor cell line

CN19 Ezio Fasoli, Ph.D., Ezio Fasoli, University of Puerto Rico at Humacao, Inhibitors of urokinase type plasminogen activator and cytostatic activity from crude plants extracts

CN20 Qin, M.D., Ph.D., Zhiqiang, Louisiana State University Health Sciences Center – New Orleans, Targeting the amino acid transporter xCT for the treatment of HIV-associated lymphoma

CN21 Adelmund, Steven, Louisiana State University Shreveport, Identification of Fusarochromanone’s Biological Targets Through Photoaffinity Labeling

CN22 Simon, Emily, University of Arkansas for Medical Sciences, Development of Recombinant Reovirus as a Therapeutic for Lung Cancer

CN23 Wang, Hongyuan, Department of Statistics, University of Kentucky, Novel Image Markers for Non-small Cell Lung Cancer Classification and Survival Prediction

CN24 Yang, Yuchen, Department of Statistics, University of Kentucky, LC-Morph: A Morphological Image Signature for Predicting Lung Cancer Survival

CN25 Williams, Amber, LSU Shreveport, cDNA Microarray Analysis of the Effects of Fusarochromanone in Human Bladder Carcinoma Cells and Budding Yeast

CN26 Suárez-Arroyo, Ivette, Universidad Central del Caribe - School of Medicine, Identification and quantification of plasma membrane proteome of IBC and non-cancerous mammary epithelial cells using SILAC

CN27 Koppolu, Bhanu prasanth, University of Arkansas, Single-step purification of recombinant interleukin-12

CN28 Kanthal, Shanthi, University of Louisiana at Monroe, Structure-activity relation of D-aminoacid containing peptidomimetics for inhibition of protein-protein interactions of EGFRs

CN29 Ghai, Pooja, Arkansas State University, Isoform-specific roles for Akt1 and Akt2 in the invasiveness of pancreatic cancer

CN30 Zhang, Haitao, Arkansas State University, Exploring the role of the actin regulatory protein CAP1 in the motility and invasion of breast cancer cells

CN31 LaFranzo, Ph.D., Natalie A., Cofactor Genomics, Cofactor Genomics: Providing Next-Gen Sequencing support to IDeA and INBRE researchers

CN32 Rachal, Peyton, Louisiana State University Shreveport, Spectroscopic Analysis of Fusarochromanone: A Potential Anti-Cancer Agent
Abstract Index

By Thematic Areas

**Cardiovascular Research**

**CV01** Prieto, M.D., Ph.D., Minolfa C., Tulane University, School of Medicine, *Deletion of prorenin receptor in the collecting duct attenuates blood pressure in angiotensin II hypertensive mice*

**CV02** Pouncey, Dakota, Hendrix College, *Identifying Potential R/S-Warfarin Metabolite Biomarkers to Improve Anticoagulant Dosing Strategies in Children*

**CV03** Stamp-Siegfried, Rachel N., University of Arkansas for Medical Sciences, College of Medicine, *Effects of Daily Kangaroo Care on Cardiorespiratory Parameters in Preterm Infants*

**CV04** Bishop, Sarah, Ouachita Baptist University, *Protective effects of aqueous extract of Terminalia arjuna bark against doxorubicin-induced cardiotoxicity*

**CV05** Santanam, Ph.D., MPH, Nalini, Joan C Edwards School of Medicine, Marshall University, Huntington, WV, *Perivascular Fat Relation to Hypertension and Coronary Artery Disease*

**CV06** Gemene, Ph.D., Kebede, Northern Kentucky University, *Simple and rapid simultaneous measurement of potassium in plasma and red blood cells as a biochemical marker for hypertension*

**CV07** Kapusta, Ph.D., Daniel R., Louisiana State University Health Science Center, *Radiofrequency Renal Nerve Ablation Attenuates Hypertension in Spontaneously Hypertensive Rats (SHR)*

**CV08** Cui, Ph.D., Taixing, University of South Carolina, *Isolation of a natural Nrf2 activator from American ginseng*

**CV09** Fleming, J. Daniel, University of Central Arkansas, *The effect of low plasma estrogen on mesenteric arterial function in female mice*

**CV10** Desai, Aesha, Robinson, Evan, Clemson University, *Effects of Blocking Cell-Cell and Cell-Matrix Interactions on Mechanical Properties of Cardiomyocytes*

**CV11** Moussa, Mohamed Idrissa Moussa, University of Central Arkansas, *Estrogen-mediated mechanisms for the regulation of voltage-gated, calcium channels in coronary arteries*

**Cell Signalling**

**CS01** Zhou, Ph.D., Guo-Lei, Arkansas State University, *GSK3 phosphorylates the actin regulatory protein CAP1 to control the actin cytoskeleton and cell polarization*

**CS02** Horton, Timothy M., Ouachita Baptist University, *Inhibiting recognition of the B-cell receptor by the tyrosine kinase Syk*

**CS03** Stahl, James A., University of Arkansas for Medical Sciences, *Global phosphoproteomic analyses define host signaling networks usurped for gammaherpesvirus replication*
Abstract Index

By Thematic Areas

General Biomedical Sciences

CS04 Sifford, Jeffrey, University of Arkansas for Medical Sciences, Productive MHV68 infection compromises the cellular p53 signaling pathway

CS05 Galperin, Ph.D., Emilia, University of Kentucky, HUWE1 is a molecular link controlling RAF-1 activity supported by the Shoc2 scaffold

CS06 Butler, John & Von Edwin, Kirby, Ouachita Baptist University, A Comparative Genomics Approach to Link Plant and Animal Oxidative Stress Signaling Pathways

CS07 Naylor, Ph.D., Kari, University of Central Arkansas, Mitochondrial fission and fusion in Dictyostelium discoideum: a search for proteins involved in membrane dynamics

CS08 Jayanthi, Ph.D., Srinivas, University of Arkansas, Mapping the binding site of the C-terminal domain of Alb3 on the Chromodomains of cpSRP43

CS09 Gao, Ph.D., Feng, University of Arkansas, Structural Flexibility and Allostery in cpSRP43 Revealed by Single Molecule FRET

CS10 Syed, Ph.D., Mohsin, University of Arkansas for Medical Sciences, Restoration of somatotrope function in vitro by ghrelin in male mice lacking the signaling domain of leptin receptor

CS11 Akhter, Ph.D., Noor, University of Arkansas for Medical Sciences, Little Rock, AR, Selective Ablation of Leptin Receptor JAK Binding Site in Somatotropes Alters Metabolic Status Causing Adult Onset Obesity

CS12 Childs, Ph.D., Gwen V., University of Arkansas for Medical Sciences, Selective Ablation of Leptin Receptor Signaling in Gonadotropes Reduces Serum Gonadotropins and Fertility in Female Mice

CS13 Jennings, Matthew, University of Arkansas, Investigation of the role [4Fe-4S] clusters play in RNA polymerase assembly and function

CS14 Stuart, Johnasha, University of Arkansas for Medical Sciences, Defining Mechanisms of Reovirus Cell Killing

CS15 Berbusse, Greg, University of Central Arkansas, Mitochondrial fission and fusion in Dictyostelium discoideum: a search for proteins involved in membrane dynamics

CS16 Refuge, Danielle M., University of Arkansas for Medical Sciences, RNA-seq analysis reveals the differential expression of Hoxa1 target genes in mouse ES cells in response to retinoic acid

CS17 Cragle, Chad, University of Arkansas for Medical Sciences, Musashi interacts with a large “effectome” to mediate sequence-specific mRNA translational control

CS18 Henderson, Ashley N., University of Arkansas, Influence of pH and Histidine Residues on Transmembrane Peptides

CS19 DeYoung, Lucas, John Brown University, Induction of PKC isoforms during Coxiella burnetii infection of THP-1 macrophages

CS20 Cleave, Chad, University of Arkansas for Medical Sciences, Mitochondrial fission and fusion require an intact cytoskeleton

CS21 Ejiofor, Shannon, Hendrix College, N-acetylcysteine inhibits liver mitochondrial biogenesis in rats fed alcohol chronically

Musashi interacts with a large “effectome” to mediate sequence-specific mRNA translational control

By Thematic Areas

General Biomedical Sciences

GM01 Anker, Ph.D., Jeffrey, College University, Luminescent sensing and imaging through tissue

GM02 MacNicol, Ph.D., Angus, University of Arkansas for Medical Science, A Novel Bioassay to Identify Chemical Regulators of Stem Cell Self-Renewal

GM03 Walter, Dustin, Ouachita Baptist University, A Radial Diffusion Assay for the Rapid Evaluation of Antimicrobial Peptides

GM04 Gokhale, Ameya S, University of Alabama at Monroe, Surface epitopes of CD2 protein to inhibit CD2-CD58 protein-protein interaction as therapeutic agent for arthritis

GM05 Byrum, Ph.D., Stephanie, Univ of Arkansas for Medical Sciences, Purification of a Specific Native Genomic Locus for Proteomic Analysis

GM06 Greene, Jennifer, School of Pharmacy, University of Charleston, WV, Analysis of polymeric gels for the transdermal delivery of capsaicin for the treatment of chronic low back pain

GM07 Hestekin, Ph.D., Christa, University of Arkansas, Microchannel Electrophoretic Analysis of Amyloid Protein Aggregation

GM08 Hall, M.D., Richard Whit, University of Arkansas for Medical Sciences, Telemedicine Collaboration Improves Perinatal Regionalization and Lowers Statewide Infant Mortality

GM09 Bansal, Ph.D., Vibha, University of Puerto Rico at Cayey, Effect of spacer arm length and ligand density on affinity membrane based separation

GM10 Dearolf, Ph.D., Jennifer L., Hendrix College, The effect of prenatal steroids on the fatigue resistance of the fetal guinea pig diaphragm

GM11 Shi, Ph.D., Wei, University of Arkansas, Chemistry and biology of a resin-glycoside family of natural products – ipomoeassins

GM12 MacNicol, Ph.D., Melanie C., University of Arkansas for Medical Science, Regulation of Musashi2-mediated mRNA translation in control of cell fate transitions

GM13 Janowska, Ph.D., Katarzyna, University of Arkansas, Crystal structure comparison and stability data study for apo and holo of Clostridial PKD-like domain

159
Abstract Index

By Thematic Areas

GM14  Barth, Ph.D., Jeremy L., Department of Regenerative Medicine and Cell Biology, Medical University of South Carolina, Leading-Edge Protein and Genomic Services at the MUSC Proteogenomics Facility

GM15  Guo, Ph.D., Zibiao, University of Mississippi Medical Center, The UMMC Molecular and Genomics Facility: Center for Psychiatric Neuroscience CDBE Core Component

GM16  Millett, Ph.D., Francis, University of Arkansas, Fayetteville, Photoinduced Electron Transfer in the Rb. Sphaeroides Cytochrome bc1 Complex

GM17  Satou, Ph.D., Ryousuke, Tulane University Hypertension and Renal Center of Excellence, Angiotensinogen is differentially regulated by angiotensin II and interleukin 6 in renal proximal tubular S1, S2 and S3 cells

GM18  Yates, PT,Ph.D., PCS, Charlotte C., Center for Translational Neuroscience, University of Arkansas for Medical Sciences, Safety of Noninvasive Electrical Stimulation of Acupuncture Points (NESAP) during a routine heel stick

GM19  Stewart, Ph.D., Mary, University of Arkansas at Monticello, Ribosomal Protein S6 in Growth and Tumors

GM20  Samanta, Dhritiman, The University of Southern Mississippi, Role of MSa in genetic regulation of Vancomycin resistance in Staphylococcus aureus

GM21  Brown, LaRae, University of Arkansas, Processing Site Insertions To Examine Membrane Protein Translocation Into Thylakoid Membranes

GM22  Zhang, Wenli, Louisiana Tech University, Point-of-care Microelectronic Diagnostics For Early Phase Rickettsial Infections

GM23  Raisa, Kiseleva, Clemson University, Investigation of targeting and antioxidative properties of nanoparticles loaded by SOD and SOD mimetic

GM24  Yoxtheimer, Tammy, University of Charleston School of Pharmacy, Investigation of three polymeric gels for the transdermal delivery of D-cycloserine for the treatment of anxiety disorders

GM25  Bauer, Ryan, University of Arkansas, Fayetteville, Structural and cross-linking studies of the bacterial collagenolytic mechanism

GM26  Washington, Dominique, Louisiana State University in Shreveport, The Role of Islet Transcription Factors in Endocrine Pancreas Development

GM27  Allensworth-James, Melody, University of Arkansas for Medical Sciences, Deletion of Leptin Receptors in Somatotropes Affects Neonatal Development and Metabolism, Leading to Adult-Onset Obesity

GM28  Odle, Angela K., University of Arkansas for Medical Sciences, Pituitary leptin, not adipocyte leptin, maintains somatotrope cell populations

GM29  Yactayo-Chang, Jessica P., Arkansas Biosciences Institute, Characterization of a gulonolactonase, the first enzyme involved in ascorbate biosynthesis localized in the chloroplast

GM30  Castillo Gonzalez, Sonia Elizabeth, Arkansas Biosciences Institute, Arkansas State University, Link Between Vitamin C Content and Cold Tolerance in Rice

GM31  Withdrawn

GM32  Blair, William, Arkansas State University, The Scanalyzer HTS, a powerful phenomics tool to identify salt tolerance lines within a rice diversity panel

GM33  Kompelli, Anvesh, Hendrix College, Effect of prenatal steroids on the myoglobin concentration in fetal guinea pig rectus abdominis muscles

GM34  Carr, Sarah, Ouachita Baptist University, High Fat Diet and Predisposition to Endometriosis

GM35 Vaughn, Kaleb L, Harding University, Selection of fatty acid desaturase 7 (fad7-1) single mutant plants in Arabidopsis thaliana using SNP-PCR primers

GM36  Nubundinho, Jean de Dieu, Philander Smith College, Photocatalysed [4+2] Annulation of N-Cyclobutylanilines with Alkynes


GM38  Nshuti, Leonce, Swane: The University of the South, Dissolution properties of goldenseal capsules

GM39  Gill, Nicholas P., Hendrix College, Piecing together the extraordinary DNA repair system of bdelloid rotifers

GM40  Moufarrej, Younna, Hendrix College, Developing RNAi to evaluate candidate DNA repair genes in bdelloid rotifers

GM41  Butler, Khatiana R., University of Arkansas at Pine Bluff, In-Vivo Comparative Study of Metal Complexes in Amelioration of Toxic kidney Injury

GM42  Horton, Timothy M., Ouachita Baptist University, Application of Computational Docking to Examine Metabolism of Chiral Drugs by CYP2C9

GM43  Chancellor, Shana, University of Arkansas at Monticello, A genetic approach to discern the roles of Drosophila ribosomal protein S6 and a potential snoRNA in growth defects

GM44  Jeffrey, Erin, University of Arkansas, Alkylation of Azole Derivatives

GM45  Reed, Zach, University of Arkansas at Little Rock, Interactions of histones H2A, H3 and H4 required for proper chromosome segregation during cell division
Abstract Index

By Thematic Areas

Infectious Disease/Immunology

ID01 Batra, Ph.D., Sanjay, Louisiana State University, Lipid rafts influence the formation of immunoproteasomes via RIP2/NLR pathway against Klebsiella pneumoniae

ID02 Yang, Carrie S., Hendrix College, Ibrutinib, a potential treatment for chronic Graft versus Host Disease inhibits T-helper 17 activation and release of IL-17A

ID03 Salinas, Eduardo, University of Arkansas for Medical Sciences, Enhancement of Gammaherpesvirus Productive Infection by TRIM21 as Revealed through a Proteomics-based LANA Interaction Screen

ID04 Xiang, Yun, Clemson University, A quantitative evaluation of the binding affinity between antibody decorated liposomes and the antigen using SPR

ID05 Blancett, Logan, The University of Southern Mississippi, Characterization of the nitrogen regulatory protein AREA in the dimorphic fungus Histoplasma capsulatum

ID06 Guerrero-Plata, Ph.D., Antonieta, Louisiana State University, Type III interferon response by respiratory paramyxovirus infection

ID07 Stumhofer, Jason S., University of Arkansas for the Medical Sciences, ICOS-mediated Tfh cell differentiation during Plasmodium chabaudi infection

ID08 Saied, Ahmad, Louisiana State University, Functional Hierarchy of HSV-1 Membrane Proteins in Corneal Infection and Virus Transmission to Ganglionic Neurons

ID09 Stanfield, Brent, Louisiana State University, Vaccination with the HSV-1 Attenuated Virus VC2 Protects Mice against Lethal Challenge with Virulent HSV-1 and HSV-2 strains

ID10 Sahukhal, Gyan S., University of Southern Mississippi, Defining a New Operon, msa, and its Role in Biofilm Development and Virulence

ID11 Greathouse, Ph.D., Denise, University of Arkansas, Fayetteville, Membrane Interactions and Biological Activities of Modified Antimicrobial Lactoferricin Peptides

ID12 Embers, Ph.D., M., Tulane National Primate Research Center, Tulane University, Tick-mediated Borrelia burgdorferi infection of Nonhuman Primates for Assessment of Antibiotic Efficacy

ID13 Lawrence, D.V.M., Ph.D., Mark, Mississippi State University, A New Center of Biomedical Research Excellence on Pathogen-Host Interactions at Mississippi State University

ID14 Kelley, Ph.D., Melissa D, University of Central Arkansas, 9-cis-Retinoic Acid and Troglitazone Impact Cellular Adhesion, Proliferation, and Integrin Expression in K562 Cells

ID15 Gray, Ph.D., Wayne, University of Arkansas for Medical Sciences, Construction and evaluation of a recombinant varicella vaccine expressing dengue virus antigens

ID16 Banos-Lara, Ph.D., Ma del Rocio, Louisiana State University, Activation of the Innate Immunity by Respiratory Paramyxovirus infection

ID17 Foster, Ph.D., Timothy P., Louisiana State University Health Sciences Center, Targeting Host Metabolic Pathways for Therapeutic Resolution of Virus- and Inflammation-Mediated Ocular Diseases

ID18 Batte, Justin, The University of Southern Mississippi, Molecular and phenotypic characterization of Methicillin resistant S. aureus isolates from a hospital in South Mississippi

ID19 Howard, Lacey, University of Southern Mississippi, Differential expression of histone H2B in yeast and mold morphotypes of a dimorphic pathogenic fungus Histoplasma capsulatum

ID20 Martinez-Guzman, Osmarie, University of Puerto Rico at Medical Sciences, Immunological effect of imiquimod and resiquimod in a DNA vaccination protocol with pA27L against smallpox

ID21 Ramirez, Maite, University of Puerto Rico Medical Sciences, Impact of vaccinia virus L3L gene in the immune response against smallpox, using a DNA-vaccination approach on a mouse model

ID22 Ghosh, Debopam, University of Arkansas for Medical Sciences, Induction of Lin-Sca1+c-kit- lymphoid progenitor cells in the spleen during acute infection with Plasmodium yoelii

ID23 Smith, Erin, The University of Southern Mississippi, Study of the Role of the mold-specific MS95 gene in DNA Repair in the Pathogenic, Dimorphic Fungus Histoplasma capsulatum

ID24 Piao, Boyang, Louisiana State University, Understanding the mucus production of a human respiratory paramyxovirus infection

ID25 Chen, Ph.D., Jing, Arkansas Biosciences Institute, Arkansas State University, RNA-binding protein HuR plays a role in Th17 cells for induction of experimental autoimmune encephalomyelitis
Abstract Index

By Thematic Areas

Neuroscience

NS01  MacNicol, Ph.D., Melanie C., Center for Translational Neuroscience, University of Arkansas for Medical Science, Control of neural stem cell differentiation and survival through manipulation of Musashi-mediated mRNA translation

NS02  Kiaei, Ph.D., Mahmoud, University of Arkansas for Medical Sciences, Nrf2 Activation as novel therapeutic strategy for ALS and its Neuroprotective Mechanisms in Astrocytes and Motor Neurons

NS03  Lindsey, Miki S, University of Central Arkansas, Calpain Inhibition Blocks Tributyltin Induced Neurodegeneration

NS04  Pandey, Pankaj, University of Mississippi, Utilizing the ensemble docking method for ranking and selection of representative cannabinoid receptor subtype 2 (CB2) models

NS05  Stenken, Ph.D., Julie, University of Arkansas, Microdialysis Sampling of Cytokine Cell Signaling Proteins in Neuroscience and Wound Healing Applications

NS06  Ni, Amy, Western Kentucky University, Time-course of effects of growth hormone (GH) and GH antagonist on auditory hair cell regeneration in zebrafish (Danio rerio)

NS07  Xu, Yao, University of Central Arkansas, Axon degeneration do shows apoptotic signatures

NS08  Doerksen, Ph.D., Robert J., University of Mississippi, Cannabinoid receptor 1 models for protein structure based drug design of antagonists

NS09  Roy, Ph.D., Kuldeep K., University of Mississippi, Uncovering the characteristic features of the active state 3D structure of the human cannabinoid subtype 2 receptor

NS10  Yadav, Ph.D., Shilpi, University of Arkansas for Medical Sciences, Fenofibrate extends survival in the SOD1G93A mouse model of amyotrophic lateral sclerosis

NS11 Withdrawn

NS12  Garrison, Ph.D., Kevin, University of Central Arkansas, TMS recruitment curves as a primary outcome measure for non-invasive electrical stimulation intervention

NS13  Hayar, Ph.D., Abdallah, University of Arkansas for Medical Sciences, External plexiform layer interneurons integrate synaptic inputs that are correlated with the activity of surrounding cells

NS14  Pyne, M.D., Jeff, Central Arkansas Veterans Healthcare System and University of Arkansas for Medical Sciences, Heart Rate Variability and PTSD and the Effect of Over-reporting

NS15  Kimbrell, M.D., Tim, University of Arkansas for Medical Science; Center for Translational Neurosciences; Central Arkansas VA Healthcare System, The Relationship Between Modified Stroop Effect, PTSD Symptoms and Response Style in OEF/OIF Veterans

NS16  Powell, M.D., Justin, University of Arkansas for Medical Sciences, rTMS restores functional connectivity of auditory cortex in schizophrenia with auditory hallucinations; a case study

NS17  Currey, Ph.D., Dorothy J., University of Arkansas for Medical Sciences Center for Translational Neuroscience (COBRE), Continuous EEG Monitoring in the Neonatal Intensive Care Unit: Detection and Treatment of Clinical and Subclinical Seizures

NS18  Montgomery, M.D., A.J., University of Arkansas for Medical Sciences, Comparison of infarct volume and neurological functions at 6 and 24 hours in a rat model of stroke

NS19  Arthur, Ph.D., M.C., University of Arkansas for Medical Sciences, Dodecafluoropentane (DDFP) tissue distribution following multiple doses of emulsion in the New Zealand white rabbit

NS20  Brown, Ph.D., A.T., University of Arkansas for Medical Sciences, Dodecafluoropentane Emulsion Reduces Brain Infarct Volume and Neurological Deficit in a Sprague Dawley Rat Stroke Model

NS21  Paul, Ph.D., Ian A., University of Mississippi Medical Center, The Animal Behavior Core (ABC) of the COBRE Center for Psychiatric Neuroscience (CPN)

NS22  Mancino, M.D., Erick, University of Arkansas for Medical Sciences, Sadness, Suicide, and Drug Misuse: Results from the Youth Risk Behavior Survey
Abstract Index

By Thematic Areas

NS29 Messias, M.D., Erick, University of Arkansas for Medical Sciences, Association Between Risky Sexual Behavior and Suicidality Among Teens in the Youth Risk Behavioral Survey

NS30 Messias, M.D., Erick, University of Arkansas for Medical Sciences, School bullying and Cyberbullying as risk factor for suicidality among US high school students: results from the 2011 YRBS

NS31 Messias, M.D., Erick, University of Arkansas for Medical Sciences, Safety and Feasibility of transcranial magnetic stimulation (rTMS) for auditory hallucinations in schizophrenia

NS32 Skinner, Ph.D., Robert D., University of Arkansas for Medical Sciences, Decreased Infarct Volume in a Rabbit Ischemic Stroke Model Following Treatment with Dodecafluoropentane Emulsion

NS33 Kane, Ph.D., Cynthia, University of Arkansas for Medical Sciences, Role of MYD88 Signaling in Ethanol Induced Immune Response in Adult Mouse Brain

NS34 Kane, Ph.D., Cynthia, University of Arkansas for Medical Sciences, Immune response to alcohol in the adolescent and adult mouse brain

NS35 Rajkowska, Ph.D., Grazyna, Department of Psychiatry & Human Behavior, University of Mississippi Medical Center, Jackson 39216, The Imaging Core Facility of the COBRE Center for Psychiatric Neuroscience

NS36 Mitchell Ph.D., Anita, University of Arkansas for Medical Sciences, Does daily kangaroo care provide sustained pain & stress relief in preterm infants?

NS37 Gadepalli, Veena, University of Mississippi, Docking studies on Leonotis leonurus and Leonurus cardiaca derived compounds for their potential activity at CB1

NS38 Bow, Eric, Department of Medicinal Chemistry, University of Mississippi, Novel benzopyran and benzoafuran scaffolds targeting the cannabinoid receptors

NS39 Garcia-Rill, E., Center for Translational Neuroscience, University of Arkansas for Medical Sciences, Novel treatment for schizophrenia

NS40 Batarseh, Yazan, College of Pharmacy, University of Louisiana at Monroe, Characterization of beta amyloid clearance by mouse cortical astrocytes

NS41 Bin Lin, Xiong, University of Arkansas for Medical Sciences, The fine temporal structure of the rat licking pattern: What causes the variability in the interlick intervals?

NS42 House, Taylor, University of Arkansas for Medical Sciences, Change in risk perception among parents of ATV users

NS43 Mohamed, Loqman A., College of Pharmacy, Department of Basic Pharmaceutical Sciences, University of Louisiana at Monroe, Involvement of P-glycoprotein in the Hepatobiliary Disposition and Blood Brain Barrier Transport of Tacrine

NS44 Qosa, Hisham, College of Pharmacy, University of Louisiana at Monroe, Characterization of amyloid-β cerebral clearance across mouse and human blood-brain barrier models

NS45 Hyatt, William S, University of Arkansas for Medical Sciences, Emerging arylcyclohexylamine drugs of abuse: drug discrimination, locomotor activity and thermoregulation

NS46 Marshall, Ramey L, University of Arkansas for Medical Sciences, In vivo effects of synthetic cannabinoids JWH-018 and JWH-073 versus Δ9-THC: inhalation versus intraperitoneal injection

NS47 Gannon, Brenda M, University of Arkansas for Medical Sciences, Monoamine transporter mediated in vivo effects of abused “bath salt” constituent M.D.PV in mice

NS48 Norwood, Andrew P, University of Arkansas for Medical Sciences, Effects of neonatal visceral pain on morphine tolerance, dependence, and withdrawal in rats

NS49 Luster, Brennon, University of Arkansas for Medical Sciences, Visualizing P/Q- and N-type calcium channels in the pedunculopontine nucleus

NS50 Hyde, James, University of Arkansas for Medical Sciences, Calcium mediated sub-threshold oscillations in the pedunculopontine nucleus using a novel ratiometric imaging technique

NS51 D’Onofrio, Stasia, University of Arkansas for Medical Sciences, Effect of Modafinil on P/Q-type calcium channel-dependent oscillations in the PPN

NS52 Kuzunovic, N., University of Arkansas for Medical Sciences, Muscarinic modulation of gamma band calcium channel-dependent activity in the pedunculopontine nucleus (PPN)

NS53 Beck, P., University of Arkansas for Medical Sciences, Mechanism of leptin action on arousal

NS54 Koo, Jenny, University of Arkansas, Effects of ApoE, Reelin, and IL-4 on Mitochondrial Respiratory Gene Expression as a Model for the Neuropathology of Alzheimer

NS55 Shrum, Stephen A., Hendrix College, Determining the Role of Neurogenin1 in the Development of the Mouse Dorsal Root Ganglion

NS56 Wolfe, Kaleb H., Hendrix College, Conditional Lineage Tracing in the Mouse Dorsal Root Ganglion

NS57 Key, Kelin, University of Arkansas at Pine Bluff, Characterization of Active Transporter Systems at Blood-Brain Barrier

NS58 Lee, Kameron, University of Arkansas at Pine Bluff, Characterization of Na+Dependent Dicarboxylate Transporter (NaDC) in Bovine Brain Microvessel Endothelial Cells (BBMEC)
Abstract Index

Alphabetical by Presenter

CN21 Adelmund, Steven, Louisiana State University Shreveport, Cancer, INBRE
CS11 Akhter, Ph.D., Noor, Ph.D., University of Arkansas for Medical Sciences, Cell Signalling, COBRE
GM27 Allensworth-James, Melody, University of Arkansas for Medical Sciences, General Biomedical Sciences, COBRE
GM01 Anker, Ph.D., Jeffrey, Clemson University, General Biomedical Sciences, COBRE
NS19 Arthur, Ph.D., M.C., University of Arkansas for Medical Sciences, Neuroscience, COBRE
ID16 Banos-Lara, Ph.D., Ma, del Rocio, Louisiana State University, Infectious Disease/Immunology, COBRE
GM09 Bansal, Ph.D., Vibha, University of Puerto Rico at Cayey, General Biomedical Sciences, INBRE
CN16 Barletta, Ph.D., Gabriel, University of Puerto Rico - Humacao, Cancer, INBRE
GM14 Barth, Ph.D., Jeremy L., Medical University of South Carolina, General Biomedical Sciences, COBRE
NS40 Batarseh, Yazan, University of Louisiana at Monroe, Neuroscience, INBRE
ID01 Batra, Ph.D., Sanjay, Louisiana State University, Infectious Disease/Immunology, COBRE
ID18 Batte, Justin, University of Southern Mississippi, Infectious Disease/Immunology, INBRE
GM25 Bauer, Ryan, University of Arkansas, Fayetteville, General Biomedical Sciences, COBRE
BI01 Bauer, Ph.D., Michael, University of Arkansas for Medical Sciences, Bioinformatics, INBRE/COBRE
NS53 Beck, P., University of Arkansas for Medical Sciences, Neuroscience, COBRE
CS15 Berbusse, Greg, University of Central Arkansas, Cell Signalling, INBRE
NS41 Bin Lin, Xiong, University of Arkansas for Medical Sciences, Neuroscience, COBRE
CV04 Bishop, Sarah, Ouachita Baptist University, Cardiovascular, INBRE
GM32 Blair, William, Arkansas State University, General Biomedical Sciences, INBRE
ID05 Blanchett, Logan, University of Southern Mississippi, Infectious Disease/Immunology, INBRE
NS38 Bow, Eric, University of Mississippi, Neuroscience, COBRE
BI20 Brochhausen, Ph.D., Mathias, University of Arkansas for Medical Sciences, Bioinformatics, INBRE
GM21 Brown, LaRae, University of Arkansas, Fayetteville, General Biomedical Sciences, COBRE
NS20 Brown, Ph.D., A.T., University of Arkansas for Medical Sciences, Neuroscience, COBRE
CN39 Burks, Jared, Arkansas State University, Cancer, INBRE
BI18 Burroughs, Mallory, Ouachita Baptist University, Bioinformatics, INBRE
GM41 Butler, Khatiana R., University of Arkansas at Pine Bluff, General Biomedical Sciences, INBRE
CS06 Butler, John &., Von Edwards, Kirby, Ouachita Baptist University, Cell Signalling, INBRE
GM05 Byrum, Ph.D., Stephanie, University of Arkansas for Medical Sciences, General Biomedical Sciences, COBRE
GM34 Carr, Sarah, Ouachita Baptist University, General Biomedical Sciences, INBRE
GM30 Castillo Gonzalez, Sonia Elizabeth, Arkansas Biosciences Institute, Arkansas State University, General Biomedical Sciences, INBRE
GM43 Chancellor, Shana, University of Arkansas at Monticello, General Biomedical Sciences, INBRE
CN09 Chavan, Ph.D., Shweta, University of Arkansas for Medical Sciences, Cancer, INBRE
ID25 Chen, Ph.D., Jing, Arkansas Biosciences Institute, Arkansas State University, Infectious Disease/Immunology, INBRE
CS12 Childs, Ph.D., Gwen V., University of Arkansas for Medical Sciences, Cell Signalling, INBRE/COBRE
CS20 Cleavenger, Jordyn, University of Central Arkansas, Cell Signalling, INBRE
BI29 Cole, Casey, University of South Carolina, Bioinformatics, INBRE
BI11 Crabtree, Nathan, University of Arkansas Little Rock and University of Arkansas for Medical Sciences, Bioinformatics, INBRE
CS17 Cragle, Chad, University of Arkansas for Medical Sciences, Cell Signalling, COBRE/INBRE
BI02 Crossley, Ph.D., David, Alcorn State University, Bioinformatics, INBRE
CV08 Cui, Taixing, University of South Carolina, Cardiovascular, COBRE
NS17 Currey, Ph.D., Dorothy J, University of Arkansas for Medical Sciences Center for Translational Neuroscience, Neuroscience, COBRE
NS51 D’Onofrio, Stasia, University of Arkansas for Medical Sciences, Neuroscience, COBRE
CS19 DeYoung, Lucas, John Brown University, Cell Signalling, INBRE
GM10 Dearolf, Jennifer L., Hendrix College, General Biomedical Sciences, INBRE
CV10 Desai, Aesha, Robinson, Evan, Clemson University, Cardiovascular, INBRE
CN15 Dhamad, Ahmed E., University of Arkansas, Fayetteville, Cancer, COBRE
NS08 Doerksen, Ph.D., Robert J., University of Mississippi, Neuroscience, COBRE
CS21 Ejiofor, Shannon, Hendrix College, Cell Signalling, INBRE
ID12 Embers, Ph.D., M., Tulane National Primate Research Center, Tulane University, Infectious Disease/Immunology, COBRE
BI06 Embry, C. Stephen, University of Arkansas for Medical Sciences/University of Arkansas at Little Rock, Bioinformatics, INBRE
BI07 Fahim, Arjang, University of South Carolina, Bioinformatics, INBRE
CN19 Fasoli, Ph.D., Fasoli, University of Puerto Rico at Humacao, Cancer,
CV09 Fleming, J. Daniel, University of Central Arkansas, Cardiovascular, INBRE
ID17 Foster, Ph.D., Timothy P., Louisiana State University Health Science Center, Infectious Disease, COBRE
BI21 Furr, Mercedes, University of Arkansas, Fayetteville, Bioinformatics, COBRE
Abstract Index

Alphabetical by Presenter

NS37  Gadeppalli, Veena, University of Mississippi, Neuroscience, COBRE
CS05  Galperin, Ph.D., Emilia, University of Kentucky, Cell Signalling, COBRE
NS47  Gannon, Brenda M, University of Arkansas for Medical Sciences, Neuroscience, COBRE
CS09  Gao, Ph.D., Feng, University of Arkansas, Fayetteville, Cell Signalling, COBRE
NS39  Garcia-Rill, E., Center for Translational Neuroscience, University of Arkansas for Medical Sciences, Neuroscience, COBRE
NS12  Garrison, Ph.D., Kevin, University of Central Arkansas, Neuroscience, INBRE
CV06  Gemene, Ph.D., Kebede, Northern Kentucky University, Cardiovascular, INBRE
CN29  Ghai, Pooja, Arkansas State University, Cancer, INBRE
ID22  Ghosh, Debopam, University of Arkansas for Medical Sciences, Infectious Disease/Immunology, COBRE
CN36  Gibson, Justin T., Northern Kentucky University, Cancer, INBRE
GM39  Gill, Nicholas P., Hendrix College, General Biomedical Sciences, INBRE
BI14  Glazko, Ph.D., Galina, University of Arkansas for Medical Sciences, Bioinformatics, INBRE
GM04  Gokhale, Ameya S, University of Louisiana at Monroe, General Biomedical Sciences, INBRE
CN13  Govindarajan, Ph.D., Mugunthan, University of Arkansas, Fayetteville, Cancer, COBRE
CN40  Gray, Raven & Scales, LaQualane, University of Arkansas for Medical Sciences, Cancer, INBRE
ID15  Gray, Ph.D., Wayne, University of Arkansas for Medical Sciences, Infectious Disease/Immunology, COBRE
ID11  Greathouse, Ph.D., Denise, University of Arkansas, Fayetteville, Infectious Disease/Immunology, INBRE/COBRE
GM06  Greene, Jennifer, School of Pharmacy, University of Charleston, General Biomedical Sciences, INBRE
CN35  Grillot, Juliana, University of Arkansas, Fayetteville, Cancer, INBRE
CN02  Grimes, Stuart, Clemson University, Cancer, COBRE
ID06  Guerrero-Plata, Ph.D., Antonieta, Louisiana State University, Infectious Disease/Immunology, INBRE/COBRE
GM15  Guo, Ph.D., Zibiao, University of Mississippi Medical Center, General Biomedical Sciences, INBRE
GM08  Hall, M.D., Richard Whit, University of Arkansas for Medical Sciences, General Biomedical Sciences, COBRE
CN44  Hardy, Drake, Ouachita Baptist University, Cancer, INBRE
NS13  Hayar, Ph.D., Abdallah, University of Arkansas for Medical Sciences, Neuroscience, COBRE
CS18  Henderson, Ashley N., University of Arkansas, Fayetteville, Cell Signalling, INBRE
CN04  Hensley, Ph.D., Lori L., Ouachita Baptist University, Cancer, INBRE
GM07  Hestekin, Ph.D., Christa, University of Arkansas, Fayetteville, General Biomedical Sciences, COBRE
BI13  Hofmann, Emily, Northern Kentucky University, Bioinformatics, INBRE
BI28  Hogan, M.D., M.S., William R., University of Arkansas for Medical Sciences, Bioinformatics, INBRE
CS02  Horton, Timothy M., Ouachita Baptist University, Cell Signalling, INBRE
GM42  Horton, Timothy M., Ouachita Baptist University, General Biomedical Sciences, INBRE
NS42  House, Taylor, University of Arkansas for Medical Sciences, Neuroscience, COBRE
ID19  Howard, Lacey, University of Southern Mississippi, Infectious Disease/Immunology, INBRE/COBRE
NS45  Hyatt, William S, University of Arkansas for Medical Sciences, Neuroscience, COBRE
NS50  Hyde, James, University of Arkansas for Medical Sciences, Neuroscience, COBRE
BI10  Jaiswal, Mihir, University of Arkansas for Medical Sciences/University of Arkansas at Little Rock, Bioinformatics, INBRE
GM13  Janowska, Ph.D., Katarzyna, University of Arkansas, Fayetteville, General Biomedical Sciences, INBRE/COBRE
CS08  Jayanthi, Ph.D., Srinivas, University of Arkansas, Fayetteville, Cell Signalling, COBRE
GM44  Jeffrey, Erin, University of Arkansas, Fayetteville, General Biomedical Sciences, COBRE
CS13  Jennings, Matthew, University of Arkansas, Fayetteville, Cell Signalling, COBRE
CN05  Johann, Jr., Ph.D., Donald J., University of Arkansas for Medical Sciences, Cancer, INBRE/COBRE
NS33  Kane, Ph.D., Cynthia, University of Arkansas for Medical Sciences, Neuroscience, COBRE
NS34  Kane, Ph.D., Cynthia, University of Arkansas for Medical Sciences, Neuroscience, COBRE
CN28  Kanthala, Shanthi, University of Louisiana at Monroe, Cancer, INBRE
CV07  Kapusta, Ph.D., Daniel R., Louisiana State University Health Science Center, Cardiovascular, COBRE
ID14  Kelley, Ph.D., Melissa D, University of Central Arkansas, Infectious Disease/Immunology, INBRE
NS57  Key, Kelin, University of Arkansas at Pine Bluff, Neuroscience, INBRE
NS52  Kezunovic, N., University of Arkansas for Medical Sciences, Neuroscience, COBRE
NS02  Kiaei, Ph.D., Mahmoud, University of Arkansas for Medical Sciences, Neuroscience, COBRE
BI23  Kilgore, Ph.D., Phillip C. S. R., Louisiana State University Shreveport, Bioinformatics, INBRE
NS15  Kimbrell, M.D., Tim, University of Arkansas for Medical Sciences; Center for Translational Neurosciences; Central Arkansas VA Healthcare System, Neuroscience, COBRE
GM33  Komppelli, Anvesh, Hendrix College, General Biomedical Sciences, INBRE
NS54  Koo, Jenny, University of Arkansas, Fayetteville, Neuroscience, INBRE
## Abstract Index

### Alphabetical by Presenter

| CS01 | MacNicol, Ph.D., Melanie C., University of Arkansas for Medical Science, Neuroscience, COBRE |
| CN18 | Kumar, Ph.D., Ajay, School of Environmental Affairs, Universidad Metropolitana, Cancer, INBRE |
| CN31 | LaFranzo, Natalie A., Cofactor Genomics, Cancer, INBRE |
| ID13 | Lawrence, D.V.M., Ph.D, Mark, Mississippi State University, Infectious Disease/Immunology, COBRE |
| NS58 | Lee, Kameron, University of Arkansas at Pine Bluff, Neuroscience, INBRE |
| CN11 | Liu, Ph.D., Jia, University of Arkansas for Medical Sciences, Cancer, COBRE |
| BI16 | Luo, Heng, University of Arkansas at Little Rock, Bioinformatics, INBRE |
| NS49 | Luster, Brennon, University of Arkansas for Medical Sciences, Neuroscience, COBRE |
| NS01 | MacNicol, Ph.D., Melanie C., University of Arkansas for Medical Science, Neuroscience, COBRE |
| GM12 | MacNicol, Ph.D., Melanie C., University of Arkansas for Medical Sciences, General Biomedical Sciences, COBRE |
| GM02 | MacNicol, Ph.D., Angus, University of Arkansas for Medical Sciences, General Biomedical Sciences, COBRE |
| CN43 | Mack, Franshawn, South Carolina State University, Cancer, INBRE |
| NS22 | Mancino, M.D., M.J, University of Arkansas for Medical Sciences, Neuroscience, COBRE |
| NS46 | Marshall, Ramey L, University of Arkansas for Medical Sciences, Neuroscience, COBRE |
| CN14 | Martin, Ph.D., Karen H, West Virginia University, Cancer, COBRE |
| ID20 | Martinez-Guzmán, Osmarie, University of Puerto Rico at Medical Science Campus, Infectious Disease/Immunology, INBRE |
| BI04 | McFarland, Devaun, University of South Carolina, Bioinformatics, INBRE |
| CN41 | McGehee, Nicole S. & Eldridge, Jacqueline D., University of Arkansas for Medical Sciences, Cancer, INBRE |
| CN38 | McNeill, Tyana D., South Carolina State University, Cancer, INBRE |
| NS28 | Messias, M.D., Erick, University of Arkansas for Medical Sciences, Neuroscience, COBRE |
| NS29 | Messias, M.D., Erick, University of Arkansas for Medical Sciences, Neuroscience, COBRE |
| NS30 | Messias, M.D., Erick, University of Arkansas for Medical Sciences, Neuroscience, COBRE |
| NS31 | Messias, M.D., Erick, University of Arkansas for Medical Sciences, Neuroscience, COBRE |
| BS17 | Meyer, Jessie, Ouachita Baptist University, Bioinformatics, INBRE |
| GM16 | Millett, Francis, University of Arkansas, Fayetteville, General Biomedical Sciences, COBRE |
| NS36 | Mitchell Ph.D., Anita, University of Arkansas for Medical Sciences, Neuroscience, COBRE |
| NS43 | Mohamed, Loqman A., University of Louisiana at Monroe, Neuroscience, INBRE |
| NS18 | Montgomery, M.D., J.A., University of Arkansas for Medical Sciences, Neuroscience, COBRE |
| GM40 | Moufarrej, Younna, Hendrix College, General Biomedical Sciences, INBRE |
| CV11 | Moussa, Mohamed Idrissa Moussa, University of Central Arkansas, Cardiovascular, INBRE |
| NS26 | Mulkey, M.D., Sarah B, University of Arkansas for Medical Sciences Center for Translational Neuroscience, Neuroscience, COBRE |
| CN12 | Murphy, Ph.D., E. Angela, University of South Carolina, Cancer, COBRE |
| NS24 | Murray, Ph.D., Richard, Hendrix College, Neuroscience, INBRE |
| BI12 | Nalabuthula, Ph.D., Narismha, University of Kentucky, Bioinformatics, COBRE |
| CS07 | Naylor, Ph.D., Kari, University of Central Arkansas, Cell Signalling, INBRE |
| NS06 | Ni, Amy, Western Kentucky University, Neuroscience, INBRE |
| NS48 | Norwood, Andrew P, University of Arkansas for Medical Sciences, Neuroscience, COBRE |
| GM38 | Nshuti, Leonce, Sewanee, The University of the South, General Biomedical Sciences, COBRE |
| GM36 | Nubudinho, Jean de Dieu, Philander Smith College, General Biomedical Sciences, INBRE |
| GM28 | Odle, Angela K., University of Arkansas for Medical Sciences, General Biomedical Sciences, COBRE |
| CN17 | Ontko, Ph.D., Allyn, Arkansas State University, Cancer, INBRE |
| CN33 | Palyok, Phillip, Louisiana State University in Shreveport, Cancer, INBRE |
| NS04 | Pandey, Pankaj, University of Mississippi, Neuroscience, COBRE |
| NS21 | Paul, Ph.D., Ian A., University of Mississippi Medical Center, Neuroscience, COBRE |
| BI19 | Perry, Jr., Ph.D., Martin D., Ouachita Baptist University, Bioinformatics, INBRE |
| BI05 | Peterson, Ph.D., Erich, University of Arkansas for Medical Sciences, Bioinformatics, COBRE |
| CN03 | Phelps, Greg, Arkansas State University, Cancer, INBRE |
| ID24 | Piao, Boyang, Louisiana State University, Infectious Disease/Immunology, INBRE |
| CV02 | Poucemy, Dakota, Hendrix College, Cardiovascular, INBRE |
| NS16 | Powell, M.D., Justin, University of Arkansas for Medical Sciences, Neuroscience, COBRE |
| GM37 | Preston, Kyle M., University of Central Arkansas, General Biomedical Sciences, INBRE |
| CV01 | Prieto, M.D., Ph.D., Minofa C., Tulane University, Cardiovascular, COBRE |
| NS14 | Pyne, M.D., Jeff, Central Arkansas Veterans Healthcare System & University of Arkansas for Medical Sciences, Neuroscience, COBRE |
| CN20 | Qin, M.D., Ph.D., Zhiqiang, Louisiana State University Health Science Center, Cancer, COBRE |
| NS44 | Qosa, Hisham, University of Louisiana at Monroe, Neuroscience, INBRE |
Abstract Index

Alphabetical by Presenter

CN32  Rachal, Peyton, Louisiana State University Shreveport, Cancer, INBRE
GM23  Raisa, Kiseleva, Clemson University, General Biomedical Sciences, INBRE
BI27  Rajagopalan, Venkatesan, University of Arkansas, Fayetteville, Bioinformatics, COBRE
NS35  Rajkowska, Ph.D., Grazyna, University of Mississippi Medical Center, Neuroscience, INBRE
ID21  Ramirez, Maite, University of Puerto Rico Medical Sciences Campus, Infectious Disease/Immunology, INBRE
NS23  Reese, Ph.D., Nancy B., Center for Translational Neuroscience, Neuroscience, COBRE
CS16  Refuge, Danielle M., Southern University and A & M College, Cell Signalling, INBRE
BI09  Robillard, Katelyn, Southeastern Louisiana University, Bioinformatics, INBRE
ID16  Rocio Banos-Lara, Ph.D., Ma del, Louisiana State University, Infectious Disease/Immunology, COBRE
CN06  Rodriguez-Dévora, Ph.D., Jorge I., Clemson University, Cancer, INBRE
NS09  Roy, Ph.D., Kuldeep K., University of Mississippi, Neuroscience, COBRE
BI08  Saha, Somdutta, University of Arkansas for Medical Sciences/University of Arkansas at Little Rock, Bioinformatics, INBRE
BI24  Saha, Rinku, University of Arkansas for Medical Sciences/University of Arkansas at Little Rock, Bioinformatics, INBRE
ID10  Sahukhal, Gyan S., University of Southern Mississippi, Infectious Disease/Immunology, INBRE
ID08  Saiied, Ahmad, Louisiana State University, Infectious Disease/Immunology, COBRE
CN10  Sakon, Ph.D., Joshua, University of Arkansas, Fayetteville, Cancer, COBRE
ID03  Salinas, Eduardo, University of Arkansas for Medical Sciences, Infectious Disease/Immunology, COBRE
GM20  Samanta, Dhiriman, University of Southern Mississippi, General Biomedical Sciences, INBRE
CV05  Santanam, Ph.D., M.P.H., Nalini, Marshall University, Cardiovascular, INBRE
GM17  Satou, Ph.D., Ryousuke, Tulane University Hypertension and Renal Center of Excellence, General Biomedical Sciences, COBRE
CN01  Satyanarayanaojis, Ph.D., Seetharama, University of Louisiana at Monroe, Cancer, INBRE
BI03  Schrader, Sarah M., Western Kentucky University, Bioinformatics, INBRE
CN37  Sevila, Gabrielle Rexy I., Northern Kentucky University, Cancer, INBRE
BI26  Shen, Shu, University of Kentucky, Bioinformatics, INBRE
GM11  Shi, Ph.D., Wei, University of Arkansas, Fayetteville, General Biomedical Sciences, COBRE
NS55  Shrum, Stephen A., Hendrix College, Neuroscience, INBRE
CS04  Sifford, Jeffrey, University of Arkansas for Medical Sciences, Cell Signalling, COBRE
CN22  Simon, Emily, University of Arkansas for Medical Sciences, Cancer, COBRE
NS32  Skinner, Ph.D., Robert D., University of Arkansas for Medical Sciences, Neuroscience, INBRE
ID23  Smith, Erin, University of Southern Mississippi, Infectious Disease/Immunology, INBRE
CN34  Soto, Israel, Louisiana State University Shreveport, Cancer, INBRE
CS03  Stahl, James A., University of Arkansas for Medical Sciences, Cell Signalling, COBRE
CV03  Stamp-Siegfried, Rachel N, University of Arkansas for Medical Sciences, Cardiovascular, COBRE
ID09  Stanfield, Brent, Louisiana State University, Infectious Disease/Immunology, COBRE
NS05  Stenken, Ph.D., Julie, University of Arkansas, Fayetteville, Neuroscience, COBRE
GM19  Stewart, Ph.D., Mary, University of Arkansas at Monticello, General Biomedical Sciences, INBRE
NS27  Stockmeier, Ph.D., Craig, University of Mississippi Medical Center, Neuroscience, COBRE
CN08  Strossner, Laura, Ouachita Baptist University, Cancer, INBRE
CS14  Stuart, Johnasha, University of Arkansas for Medical Sciences, Cell Signalling, COBRE
ID07  Stumhofer, Jason S., University of Arkansas for Medical Sciences, Infectious Disease/Immunology, COBRE
CN26  Suárez-Arroyo, Ivette, Universidad Central del Caribe - School of Medicine, Cancer, INBRE
CS10  Syed, Ph.D., Mohsin, University of Arkansas for Medical Sciences, Cell Signalling, COBRE
NS25  Tai, Ph.D., Sherrica, University of Arkansas for Medical Sciences, Neuroscience, COBRE
CN42  Tobaczyk, Julia, Louisiana Tech University- Ruston, Cancer, INBRE
GM35  Vaughn, Kaleb L, Harding University, General Biomedical Sciences, INBRE
BI15  Walsh, Gretchen A., Western Kentucky University, Bioinformatics, INBRE
GM03  Walter, Dustin, Ouachita Baptist University, General Biomedical Sciences, INBRE
CN23  Wang, Hongyuan, University of Kentucky, Cancer, INBRE
GM26  Washington, Dominique, Louisiana State University in Shreveport, General Biomedical Sciences, INBRE
CN07  Weed, Ph.D., Scott A., West Virginia University, Cancer, INBRE
BI25  Williams, Sara, Ouachita Baptist University, Bioinformatics, INBRE
CN25  Williams, Amber, Louisiana State University Shreveport, Cancer, INBRE
NS56  Wolfe, Kaleb H., Hendrix College, Neuroscience, INBRE
ID04  Xiang, Yun, Clemson University, Infectious Disease/Immunology, INBRE
NS07  Xu, Yao, University of Central Arkansas, Neuroscience, INBRE
Abstract Index

Alphabetical by Presenter

GM29  Yactayo-Chang, Jessica P., Arkansas Biosciences Institute, Arkansas State University, General Biomedical Sciences, INBRE
NS10  Yadav, Ph.D., Shilpi, University of Arkansas for Medical Sciences, Neuroscience, COBRE
CN24  Yang, Yuchen, University of Kentucky, Cancer, INBRE
ID02  Yang, Carrie S., Hendrix College, Infectious Disease/Immunology, INBRE
GM18  Yates, PT,Ph.D., PCS, Charlotte C., University of Arkansas for Medical Sciences, General Biomedical Sciences, COBRE
GM24  Yoxtheimer, Tammy, University of Charleston, General Biomedical Sciences, INBRE
CN30  Zhang, Haitao, Arkansas State University, Cancer, INBRE
GM22  Zhang, Wenli, Louisiana Tech University, General Biomedical Sciences, INBRE
CS01  Zhou, Ph.D., Guo-Lei, Arkansas State University, Cell Signalling, INBRE
BI12  Zybailov, Ph.D., Boris I., University of Arkansas for Medical Sciences, Bioinformatics, INBRE
2013 Southeast Regional IDeA Meeting Sponsors

National Institutes of Health (NIH)
National Institute of General Medical Sciences (NIGMS)
Institutional Development Award Program (IDeA)

Arkansas IDeA Networks of Biomedical Research Excellence
(AR INBRE)
Arkansas Center for Microbial Pathogenesis and Host Inflammatory Responses (COBRE)
Arkansas Center for Translational Neuroscience (COBRE)
Arkansas Center for Protein Structure and Function (COBRE)
University of Arkansas for Medical Sciences (UAMS)