Acknowledgements

An event of this size and scope cannot come together without the hard work and dedication of colleagues and partners throughout Emory.

First and foremost is Kathy Smith, Director of Recruitment and Admissions for the Laney Graduate School’s Graduate Division of Biological and Biomedical Sciences. Kathy coordinates and manages the application and registration processes, travel planning and conference logistics. She is likely the person you communicated with most often, and we are grateful for her skills and management in bringing this together.

Likewise, we want to thank the many Emory faculty and students who have also dedicated long hours to preparing for this event and who will dedicate even more during the symposium.

**THE SYMPOSIUM COMMITTEES:**
The 2015 Chair and Co-Chair of this event is Dr. Edward T. Morgan (Chair), Graduate Division of Biological and Biomedical Sciences – Molecular and Systems Pharmacology and Dr. James Kindt (Co-Chair), Chemistry. Professors Morgan and Kindt were assisted by subcommittees responsible for activities that ranged from recruiting symposium participants to coordinating campus tours and meetings. The chairs of these subcommittees are listed below.

– Guy Benian, Graduate Division of Biological and Biomedical Sciences – Genetics and Molecular Biology
– Ayush Kishore, Graduate Division of Biological and Biomedical Sciences – Molecular and Systems Pharmacology
– Pat Marsteller, Director, Center for Science Education
– Jeff Boatright, Department of Ophthalmology
– Hillary Rodman, Psychology

**THE SPONSORS AND PARTICIPANTS:**
We also extend our gratitude to the many offices, units and programs at Emory, as well as our external sponsors, for their financial support and participation in this event.

– Office of the Provost
– Laney Graduate School
– School of Medicine
– Rollins School of Public Health
– Emory College of Arts and Sciences
– Office of Postdoctoral Education
– Graduate Division of Biological and Biomedical Sciences
– MD/PhD Medical Scientist Training Program
– Graduate programs in Biomedical Engineering, Chemistry, Mathematics and Computer Science, Physics, Psychology and the Public Health Sciences
– Emory Initiative to Maximize Student Development (imsd) program
– Oak Ridge Associated Universities: University Partnerships
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- Poster Presentations:
  - External Presenters 19
  - Emory Presenters 71
Welcome!

Dear Friends,

On behalf of the Laney Graduate School and our partners from the School of Medicine, Emory College of Arts and Sciences, the Rollins School of Public Health, the Office of Postdoctoral Education and the Emory University Office of the Provost, I am delighted to welcome you to this year’s STEM Research and Career Symposium.

During your time here, you will connect with Emory students, researchers, and faculty who are eager to talk with you about your research, their work and professional experiences. We want to share with you our passion for what makes Emory a great place to study, train and launch your career in the STEM disciplines.

More than 110 undergraduate and graduate students from a number of schools beyond Emory, as well as 25 mentors and program directors, will be in attendance. We hope that during your visit, you will see Emory’s commitment to inclusion in the STEM disciplines and across the university.

Also joining you throughout this event are more than 100 Emory faculty and students who are eager to offer their time and look forward to meeting you and hearing about your research and interests. Together, we want to ensure that your experience at Emory is inspiring and rewarding.

We hope your connection to Emory continues beyond the closing events on March 27th. We look forward to building on the relationships that we establish with you here this week. We encourage you to reach out and expand your Emory network and continue to move toward a career in the STEM disciplines. Feel free to contact anyone from the Organizing Committee listed below.

Again, welcome to this year’s STEM Research and Career Symposium. We look forward to making this a memorable and fulfilling visit to Emory University.

Lisa A. Tedesco, PhD
Vice Provost for Academic Affairs – Graduate Studies
Dean, James T. Laney School of Graduate Studies
Professor, Rollins School of Public Health
The Organizing Committee

Mary DeLong  
Director, Office of Postdoctoral Education

Cathryn Johnson  
Senior Associate Dean, Laney Graduate School

James Kindt  
Co-Chair of Organizing Committee, Chemistry

Cora MacBeth  
Assistant Dean for Student Affairs, Laney Graduate School

Edward Morgan  
Chair of Organizing Committee,  
Graduate Division of Biological and Biomedical Sciences – Molecular Systems Pharmacology

Monya Ruffin  
Director of Education, Outreach, and Diversity, Center for Selective C-H Functionalization

Kathy Smith  
Director of Recruitment and Admissions, Graduate Division of Biological and Biomedical Sciences

Margie Varnado  
Business Manager, Graduate Division of Biological and Biomedical Sciences

Keith Wilkinson  
Director, Graduate Division of Biological and Biomedical Sciences
Opening Remarks

Kristine M. (Tina) Garza, PhD

is Associate Professor of Biological Sciences at the University of Texas at El Paso. Her research program is focused on the impact of obesity on the induction of effective T cell-mediated immunity, and the influence of nanomaterials on pulmonary microbial clearance by innate immune cells. Dr. Garza’s efforts in the training and mentoring of underrepresented minority students in STEM have been recognized regionally and nationally as a National Academies Education and Training Mentor in the Life Sciences. She was a member of the Board of Directors of SACNAS (Society for Advancement of Hispanics/Chicanos and Native Americans in Science), and recently took a one year leave of absence to serve as the Executive Director for SACNAS. She is once again conducting research, teaching new classes, and serving students through teaching and mentoring.

Dinner Speaker

Dr. Hannah Valantine, MD

is the NIH inaugural Chief Officer for Scientific Workforce Diversity, and a senior scientist in the intramural research program. She was recruited as a nationally recognized scientist to develop a comprehensive vision and strategies to diversify scientific applicant pools and pipelines, to expand recruitment methods and retention strategy, and to help promote inclusiveness and equity throughout the biomedical research community at large. Prior to starting this position in April 2014, Dr. Valantine was Professor of Cardiovascular Medicine and the Senior Associate Dean for Diversity and Leadership at Stanford School of Medicine, a leadership position she held since November 2004. She is nationally recognized for her transformative approaches to diversity, and is a recipient of the NIH Director’s Pathfinder Award for diversity in the scientific workforce.
# Schedule of Events

All Wednesday and Thursday events will take place at the Emory Conference Center. Friday’s events will take place at the Emory Conference Center and on the Emory Campus.

## Wednesday, March 25

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>4:00 – 6:00 pm</td>
<td>Registration</td>
<td>Great Hearth / Lobby</td>
</tr>
<tr>
<td>6:00 – 8:00 pm</td>
<td>Welcome Reception</td>
<td>Great Hearth / Lobby</td>
</tr>
</tbody>
</table>

## Thursday, March 26

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Location</th>
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</thead>
<tbody>
<tr>
<td>8:00 – 9:00 am</td>
<td>Registration</td>
<td>Emory Amphitheatre Foyer</td>
</tr>
<tr>
<td>8:00 – 8:45 am</td>
<td>Continental Breakfast</td>
<td>Emory Break Area</td>
</tr>
<tr>
<td>9:00 – 9:45 am</td>
<td>Keynote Speaker</td>
<td>Emory Amphitheatre</td>
</tr>
<tr>
<td>10:00 – 11:15 am</td>
<td>Student Oral Presentations 1</td>
<td>Emory Amphitheatre</td>
</tr>
<tr>
<td></td>
<td>Oral Abstracts 1 – 5</td>
<td></td>
</tr>
<tr>
<td>11:20 – 11:45 am</td>
<td>Break</td>
<td></td>
</tr>
<tr>
<td>11:45 am – 1:00 pm</td>
<td>Poster Session 1</td>
<td>Lullwater</td>
</tr>
<tr>
<td></td>
<td>Posts 1 – 68</td>
<td></td>
</tr>
<tr>
<td>1:15 – 2:45 pm</td>
<td>Lunch with Programs</td>
<td>Silverbell</td>
</tr>
<tr>
<td>3:00 – 4:15 pm</td>
<td>Poster Session 2</td>
<td>Lullwater</td>
</tr>
<tr>
<td></td>
<td>Posts 71 – 139</td>
<td></td>
</tr>
<tr>
<td>4:30 – 5:45 pm</td>
<td>Student Oral Presentations 2</td>
<td>Emory Amphitheatre</td>
</tr>
<tr>
<td></td>
<td>Oral Abstracts 6 – 10</td>
<td></td>
</tr>
<tr>
<td>6:30 – 8:30 pm</td>
<td>Dinner with Speaker</td>
<td>Salons 1 – 3</td>
</tr>
<tr>
<td></td>
<td>Hannah Valantine, MD</td>
<td></td>
</tr>
<tr>
<td>9:00 pm – 12:00 am</td>
<td>Social Event (Bowling and Billiards)</td>
<td>Wisteria Lanes</td>
</tr>
<tr>
<td></td>
<td>Mingle with Emory students, postdocs and faculty</td>
<td></td>
</tr>
</tbody>
</table>

## Friday, March 27

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:00 – 8:45 am</td>
<td>Continental Breakfast</td>
<td>Cox Hall</td>
</tr>
<tr>
<td>9:00 – 9:50 am</td>
<td>Professional Development Breakout Session</td>
<td>Cox Hall</td>
</tr>
<tr>
<td></td>
<td>4 concurrent</td>
<td></td>
</tr>
<tr>
<td>10:00 – 10:50 am</td>
<td>Professional Development Breakout Session</td>
<td>Cox Hall</td>
</tr>
<tr>
<td></td>
<td>4 concurrent</td>
<td></td>
</tr>
<tr>
<td>11:00 – 12:15 am</td>
<td>Tours for prospective students</td>
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<tr>
<td></td>
<td>Prospective postdoc faculty meetings</td>
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</tr>
<tr>
<td>11:15 am – 12:30 pm</td>
<td>Roundtable discussion with Emory faculty for advisors</td>
<td>Hotel Dining Room</td>
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<tr>
<td></td>
<td>(with lunch)</td>
<td></td>
</tr>
<tr>
<td>12:30 pm</td>
<td>Lunch and Departure</td>
<td>Cox Hall</td>
</tr>
</tbody>
</table>
Lunch is located in the Silverbell Pavilion. Find the table of interest, pick up your lunch, and enjoy.

<table>
<thead>
<tr>
<th>Programs</th>
<th>Table No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSYC Psychology</td>
<td>1</td>
</tr>
<tr>
<td>PHYS Physics</td>
<td>2</td>
</tr>
<tr>
<td>MCS Math &amp; Computer Science</td>
<td>2</td>
</tr>
<tr>
<td>CHEM Chemistry</td>
<td>3</td>
</tr>
<tr>
<td>CCHF Center for C-H Functionalization</td>
<td>3</td>
</tr>
<tr>
<td>IMSD Initiative to Maximize Student Development</td>
<td>4</td>
</tr>
<tr>
<td>BEST Broadening Experiences in Scientific Training Program</td>
<td>4</td>
</tr>
<tr>
<td>SURE Summer Undergraduate Research Experience</td>
<td>5</td>
</tr>
<tr>
<td>MSP Molecular and Systems Pharmacology</td>
<td>6</td>
</tr>
<tr>
<td>CBIO Cancer Biology</td>
<td>6</td>
</tr>
<tr>
<td>IMP Immunology and Molecular Pathogenesis</td>
<td>7</td>
</tr>
<tr>
<td>NS Neuroscience</td>
<td>8</td>
</tr>
<tr>
<td>BIOS Biostatistics</td>
<td>9</td>
</tr>
<tr>
<td>EPI Epidemiology</td>
<td>9</td>
</tr>
<tr>
<td>EHS Environmental Health Sciences</td>
<td>10</td>
</tr>
<tr>
<td>NHS Nutrition and Health Sciences</td>
<td>10</td>
</tr>
<tr>
<td>BCDG Biochemistry, Cell and Developmental Biology</td>
<td>12</td>
</tr>
<tr>
<td>GMB Genetics and Molecular Biology</td>
<td></td>
</tr>
<tr>
<td>BGSA Black Graduate Student Association</td>
<td>12</td>
</tr>
<tr>
<td>LGSA Latin Graduate Student Association</td>
<td>12</td>
</tr>
<tr>
<td>Open</td>
<td>13</td>
</tr>
<tr>
<td>MMG Microbiology and Molecular Genetics</td>
<td>14</td>
</tr>
<tr>
<td>PBEE Population Biology, Ecology and Evolution</td>
<td>14</td>
</tr>
<tr>
<td>Postdoctoral Funding</td>
<td>15</td>
</tr>
<tr>
<td>OPE Office of Postdoctoral Education</td>
<td>16</td>
</tr>
<tr>
<td>FIRST Fellowships in Research and Science Teaching</td>
<td>16</td>
</tr>
<tr>
<td>MPC Minority Postdoc Council</td>
<td>16</td>
</tr>
<tr>
<td>MD/PhD MD/PhD</td>
<td>17</td>
</tr>
<tr>
<td>Open</td>
<td>18</td>
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<td></td>
<td>19</td>
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<tr>
<td></td>
<td>20</td>
</tr>
</tbody>
</table>
Professional Development Breakout Sessions
Cox Hall
Conference rooms are on the third floor

Conference Center
### Professional Development Breakout Sessions

**March 27 · 9:00 – 9:50 am**

<table>
<thead>
<tr>
<th>Session Title</th>
<th>Audience</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>How to Prepare a Competitive Application for Graduate School</strong></td>
<td>For Current Undergraduate Students and Mentors</td>
<td>Cox Hall 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Life of a Postdoc</strong></td>
<td>For Current Graduate Students and Others</td>
<td>Cox Hall 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Research Opportunities for Undergraduates at Emory and Beyond</strong></td>
<td>For Current Undergraduate Students and Mentors</td>
<td>Cox Hall 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PhD, MD/PhD or MD?</strong></td>
<td>For current Undergraduate Students</td>
<td>Cox Hall 4</td>
</tr>
<tr>
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<td></td>
</tr>
</tbody>
</table>

**Learn more about Laney Graduate School programs and funding opportunities. Discuss GRE scores, personal statement, research opportunities, and publications to make your application competitive for graduate school.**

**Choosing a mentor or a team of mentors should be given the same consideration as choosing a life partner! It is a relationship.**

What are the advantages and disadvantages of choosing new faculty or more experienced ones? This session will discuss the process of finding a postdoc mentor as well as the typical work day and life of a postdoctoral scholar.

**Interested in Undergraduate Research? Emory offers a number of research opportunities for non-Emory undergraduate students. Find out more about the following programs:**

- Summer Undergraduate Research Experience (SURE)
- Pediatric Engineering Research Summer Experience (PERSE)
- Summer Undergraduate Program in Emory Renal Research (SUPERR)
- Center for Stereoselective C-H Functionalization (CCHF)

**There are a number of higher education options for students with bachelor’s degrees in the sciences. However, it can often be difficult to decide which program will help reach your professional goals.**

In this session, current PhD, MD/PhD and MD students will discuss the factors they considered when choosing a program of study. The panel will take questions and answers from the audience.

---

Damon Williams, organizer | Amanda James, organizer | Molly Embree, Jacob Shreckengost and Jeff Sands, organizers | Gillian Hue and Mary Horton, organizers
The Emory PhD Experience

For Undergraduate Students

Cox Hall 1

A panel of students share their experience at Emory, discuss their transition to graduate school, and discuss why they found Emory to be a good fit.

Life after Graduate School

For Current Graduate Students and Mentors

Cox Hall 2

Do you know what career options are available after getting a PhD or an MD/PhD? From academia to research to the public sector, the list of possibilities is endless.

The facts show that most advanced degree students are in a comprehensive program that can qualify them for any number of career paths both in and beyond academia. This session will address the often difficult decision-making process of whether to pursue an academic faculty career or an alternative career. In addition, this session will explore the alternative career options available after graduate school.

This session will also address a new program for Emory graduate students and post-doctoral fellows known as the BEST Program (gs. emory.edu/sites/best). The BEST program aims to better prepare pre-doctoral and postdoctoral scientists for the breadth of possible careers in the biomedical research workforce and to establish a network, share, evaluate and disseminate widely best practices for the community. The session will also have information from the Office of Postdoctoral Education.

Succeeding in a Graduate Program

For Current and Prospective Graduate Students

Cox Hall 3

This session will focus on prospective mentor questions, time management and productivity tips for good laboratory practices, as well as collaboration and networking.

Developing a Career Plan and Individual Development Plans

For Undergraduate Students, Graduate Students and Mentors

Cox Hall 4

In this session students will begin working on individual development plan questions and assessments addressing questions such as:

- What is an individual Development plan?
- What are my objectives in entering graduate school?
- What type of training do I desire?
- What are my strengths?
- What skills do I need to develop?
- What kinds of research or creative projects will engage me?
- How much independent versus team work do I want to do?
- What type of career do I want to pursue?
- What are your short-term career goals?
- How will you achieve these goals within the next two to five years?
- What are your long-term career goals?

Students will begin to integrate questions about their ideal graduate preparation and their ideal job, such as: myidp.sciencecareers.org.

Gillian Hue and Amanda James, organizers

Mary DeLong and Gaia Vasilver-Shamis, organizers

Shawn Hochman, organizer

Pat Marsteller, organizer
Oral Presentations
Development of an Ice Replication Technique

Luis Suarez,
Sarah Brooks

Department of Atmospheric Sciences, Texas A&M University; University of Texas at El Paso

Previous work from our lab has pointed out the importance of shape in ice crystals. They are strictly tied to temperature and to the number of water molecules present. In heterogeneous freezing aerosols, also known as ice nuclei (IN), act as a form of catalyst by facilitating ice nucleation. Dust soot and pollen are the most well known IN. Although many experiments have studied the relationship between aerosols optical properties and ice crystals shapes there is limited actual images on such process. Understanding the importance in the ice crystal shapes we developed a technique to observe them by replicating them in a plastic solution. We looked at old ice crystals replication methods and tried to optimize them for relevant conditions in IN experiments. Ethylene dichloride and trichloro-ethylene were the solvents used on polystyrene and Plexiglas plastics. Concentrations around 1% by mass was found ideal for its enduring replicas and rapid formation. In future studies the optimized replication technique combined with the Continuous Flow Diffusion Chamber (CFDC) could be used to provide images of ice crystals nucleated and grown under controlled chamber conditions. These studies will help in the understanding of heterogeneous freezing.

Toward Co-catalyst Loading on Common Metal Oxides for Oxygen Evolution Reactions using NiFeOOH

Lydia Mensah,
Bart Bartlett

Department of Chemistry, University of Michigan, Ann Arbor, MI; Department of Chemistry, Xavier University of Louisiana, New Orleans, LA

The role of Fe in amplifying the catalytic activity of NiOOH for the oxygen evolution reaction (OER) has been highly debated in the literature. It is not clear whether structure or composition is altered with Fe. Nevertheless, Fe is critical for increasing the reaction rate of Ni-based oxyhydroxide electrocatalysts. If Fe doping NiOOH films improves catalytic efficiency, then finding the best Ni:Fe metal ratio for our system will guide us towards the co-catalyst that produces the largest quantity of O2. We detail electrochemical, X-ray diffraction, and O2 production measurements on control NiOOH films and on Ni1-xFexOOH thin films to analyze to correlate composition, structure, and electronic properties to the observed OER activity. The catalytic onset potential and a shift in the Ni2+/3+ redox couple after soaking films in 1 M KOH provide evidence that the crystalline layered structure is forming. Cyclic voltammetry (CV) on Ni1-xFexOOH thin films showed that 2% Fe and 5% Fe incorporation shift the catalytic onset cathodically. Each CV was carried out in 1 M KOH (pH 13.6) using FTO (fluorine-doped tin oxide), Ag/AgCl, and Pt mesh as working, reference, and auxiliary electrodes respectively. Further bulk electrolysis and O2 detection experiments were performed on FTO in 1 M KOH at 0.65 V vs. Ag/AgCl, in a two-compartment cell using Pt mesh as the auxiliary electrode.
Light-oxygen-voltage (LOV) domains are signaling modules found in photosensory proteins across Eukarya, Archea, and Bacteria. The engineered LOV domain EL222 presents itself as a possible genetic tool for controlled gene transcription with rapid activation (<10s) and deactivation (<50s) protein kinetics, making it a suitable for optogenetic control. Upon photoillumination (~450nm) EL222 forms a cysteine-flavin covalent adduct, a mechanical response within the protein leading to a dissociation of LOV domain’s Beta-sheet surface interacting with the J-alpha helix of the helix-turn-helix (HTH) domain. Prior molecular dynamic simulations lead us to believe that these interactions between the N-terminal cap and C-terminal J-alpha linker can be significantly altered by mutating the glutamine 138 in the Beta-sheet of the core EL222. These structural changes were monitored by expressing EL222 in E. coli., purified using affinity chromatography, and tryptophan as an endogenous fluorescent marker for Foster resonance energy transfer (FRET). Our data demonstrate that tryptophan is capable of measuring timing differences in the protein’s photocycle and unfolding kinetics, further showing that EL222’s ability to undergo DNA binding is delayed (~1s). We present a possible addition to EL222’s optogenetic utility, thus broadening its application as a powerful light-gated gene encryption tool.

Human eyes contain abundant amounts of crystallin proteins. Crystallins can undergo both aggregation and phase separation, which can alter the transparency of the lens and cause cataracts, underlining the biological relevance and importance of understanding crystallin interactions. Currently, our research focuses on Bovine Gamma B Crystallin (CRYGB). We have genetically engineered two versions of recombinant CRYGB protein, one with a hexahistidine (His) tag and one without, and have successfully expressed them in Escherichia coli. The 2D 15N-1H correlation nuclear magnetic resonance (NMR) spectrum of His-tagged CRYGB suggests that the His tag alters the structure and/or dynamics of CRYGB. The NMR spectra of non-tagged CRYGB at different concentrations and temperatures point to possible changes in structure, dynamics, and/or intermolecular interactions.
Cancer Biology

Translational Regulation of the Anti-Apoptotic Protein, XIAP, in Inflammatory Breast Cancer

Courtney M. Edwards, Myron K. Evans, Gayathri R. Devi
Department of Surgery, Duke University, Durham, NC; Hampton University, Hampton, VA

Inflammatory breast cancer (IBC) is highly aggressive, lethal, and often acquires resistance to chemotherapy. IBC is characterized by the formation of hyperproliferative cell clusters termed tumor emboli. This unique pathogenic property is partly due to the overexpression of the translation initiation factor, eIF4G1. Overexpression of eIF4G1 enhances translation of mRNAs with internal ribosome entry sites (IRES). Enhanced translation may not only increase tumor emboli formation, but may also increase cancer cell survival during cellular stress when translation is normally suppressed. The overexpression of X-linked inhibitor of apoptosis protein (XIAP) also promotes cancer cell survival and may be due to enhanced translation as the 5'UTR of XIAP contains an active IRES. In this study, SUM149 cells derived from primary IBC tumors were used to determine if eIF4G1 regulates XIAP expression through IRES-mediated translation. Targeted knockdown of eIF4G1 with a specific shRNA led to a significant decrease in XIAP expression beginning 48 hours post-transfection. To assess the effect of the knockdown on tumor emboli formation, SUM149 cells were transfected with the shRNA and cultured in ultra-low attachment plates. Knockdown of eIF4G1 decreased the number and size of mammospheres formed. Lastly, to evaluate the effect of the knockdown on drug resistance, cellular viability of a resistant cell line (rSUM149) was assessed after treatment with a potent apoptosis inducer. A significant correlation was previously found between XIAP overexpression in rSUM149 cells and sensitivity to therapy-induced apoptosis. In the present study, knockdown of eIF4G1 re-sensitized rSUM149 cells to the apoptosis inducer and decreased cell viability.

Cancer Biology

Snail-mediated Cathepsin L Activity Regulates Epithelial Mesenchymal Transition and Bone Turnover

Liza Burton,1 Manu Platt,2 Camille Ragin,3 Robin Roberts,4
Valerie Odero-Marah,1

Prostate cancer (PCa) is the most frequently diagnosed cancer in African-American men and is associated with increased bone turnover. Snail, a zinc finger transcription factor, is increased in prostate cancer and is associated with increased tumor motility and invasion by induction of epithelial mesenchymal transition (EMT). Cathepsin proteases have specific roles in bone remodeling and EMT. We have shown previously that Snail promotes osteoclastogenesis in prostate cancer cells and that Snail-mediated EMT can be antagonized by muscadine grape skin extract (MSKE), a natural product rich in anthocyanin. We hypothesize that Snail regulates EMT and osteoclastogenesis via Cathepsin L activity. Initially, we examined the expression of Snail and Cathepsin L in prostate cancer cells by Western blot analysis and Cathepsin L Activity via Zymography. We observed that Snail overexpression in various prostate cancer cell lines led to increased Cathepsin L expression and activity, which could be antagonized by Stat-3 knockdown with siRNA. Using human prostate cancer tissue from the Bahamas, we stained for Snail and Cathepsin L, which revealed co-localization within the nucleus of more de-differentiated tissue samples. Cells overexpressing Snail displayed increased migration, invasion and osteoclastogenesis which could be abrogated by treatment with MSKE (5 ug/mL and 20 ug/mL) or 5 uM Z-FY-CHO Cathepsin L inhibitor. MSKE and Z-FY-CHO reverted Snail-mediated EMT by increasing E-cadherin and decreasing vimentin expression. These findings suggest that Snail increases Cathepsin L activity via Stat-3 signaling leading to EMT and osteoclastogenesis which can be abrogated by MSKE.

1 Center for Cancer Research and Therapeutic Development, Department of Biological Sciences, Clark Atlanta University, Atlanta, GA;
2 Department of Biology, Georgia Institute of Technology, Atlanta, GA;
3 Fox Chase Cancer Center, Temple Health, Philadelphia, PA;
4 University of West Indies School of Clinical Medicine and Research, Nassau, The Bahamas
A Novel Receptor Cross-talk Between Melatonin Receptor 1 and the Insulin Receptor Modulates Insulin Sensitivity

Pharmacology

Sharon Owino, Kenkichi Baba, Susana Contreras-Alcantaras, Gianluca Tosini

Department of Pharmacology & Toxicology, Morehouse School of Medicine, Atlanta, GA

Dietary-Induced Obesity Disturbs Iron Homeostasis and Alpha-Synuclein Expression in Mouse Brain

Nutrition

Aria Byrd, Keith Erikson, Justin Plummer, Jian Han

Department of Biology, North Carolina A&T State University, Greensboro, NC; Department of Nutrition, University of North Carolina at Greensboro, Greensboro, NC

Many aspects of metabolism such as circulating metabolites, hormones, and activation of metabolic pathways are linked to the circadian timing system. Disruption or misalignment of the circadian system is associated with increased risk of developing obesity, diabetes, and metabolic syndrome. Although most notably known for its function in the regulation of sleep/wake cycles; recent studies demonstrate a novel role for melatonin in the regulation of glucose metabolism. The clinical importance of these findings is highlighted by genetic studies linking polymorphisms in both melatonin receptors (MT1 and MT2) to increased risk of developing insulin resistance and type 2 diabetes. Previously we established that MT1-/- mice exhibit delayed glucose clearance and decreased sensitivity to insulin; however the mechanisms underlying this phenotype remain poorly understood. Here we demonstrate that when challenged with a high fat diet (45% kcal/fat), MT1-/- mice exhibit increased susceptibility to diet induced diabetes in the absence of increased adiposity. Furthermore, in response to insulin, MT1-/- mice display tissue specific impairments in the activation of the insulin signaling pathway. Activation of the insulin signaling pathway was assessed by quantifying levels of p-Akt and p-IRS-1 via western blot analysis. Notably, severe impairments in the activation of both Akt and IRS-1 were found within adipose tissue and liver of MT1-/- mice; with the most profound effects occurring within the liver. These data suggest that signaling through MT1 modulates insulin signaling within peripheral tissues, and for the first time highlights a critical role for MT1 in the potentiation of insulin receptor signal transduction.

Obesity has been linked with altered systemic iron biology and is a risk factor for neurodegenerative diseases such as Parkinson’s. Given that the mishandling of brain iron is associated with neurodegenerative processes, we wanted to explore the relationship between obesity and brain iron biology. The objective of this study was to examine the effects of dietary-induced obesity on brain iron, ferritin (a good indicator of iron biology) and alpha synuclein (a protein linked with neurodegenerative processes). Thirty C57BL/6J male mice were randomly assigned into 6 dietary groups with various amounts of fat (normal and high) and iron (low, normal and high) for 24 weeks. Brains were harvested and dissected into four iron rich regions (thalamus, striatum, midbrain and hippocampus) that are associated with neurodegenerative diseases. Total brain iron contents from these regions were quantified with atomic absorption spectrometry. Ferritin H (FtH) and alpha-synuclein mRNA expression was measured with quantitative real-time polymerase chain reaction analysis. FtH and alpha-synuclein protein expressions were determined with western blot analysis. The high fat diet (HFD) significantly altered brain regional iron concentrations compared to the control fat group, in the midbrain and striatum. This is in conjunction with changes in FtH and alpha-synuclein expressions. The changes observed in brain iron biology due to obesity were limited to the basal ganglia and were not present in the hippocampus. These data imply specific neurodegenerative etiologies in different brain regions.
The Role of Autophagy Proteins in *C. elegans* Presynaptic Assembly

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Autophagy is an evolutionarily conserved cellular process through which proteins and damaged organelles are degraded via a lysosomal pathway. It is especially required in post-mitotic cells, such as neurons, for cell maintenance. It has been shown that autophagy plays an important role in processes such as neurodegeneration and synaptic plasticity. These findings prompted us to question whether autophagy is required for the formation or maintenance of synapses. For our studies, we examined a neuron in the nerve ring of the nematode *C. elegans* and fluorescently labeled synaptic vesicle proteins RAB-3 and SNB-1. RAB-3 is a small GTPase that associates with synaptic vesicles, and SNB-1 is a component of the SNARE complex required for synaptic vesicle fusion. With these markers, we examined synaptic vesicle localization in autophagy pathway mutants. We identify 13 autophagy pathway components that are required for presynaptic assembly. We also showed that ATG-9, a component of the autophagy pathway, co-localizes with RAB-3 in presynaptic regions and that ATG-9 presynaptic localization is dependent on the synaptic-vesicle-specific kinesin, UNC-104. To further determine the role of autophagy in presynaptic assembly, we generated a lysosomal marker using GFP-tagged LAAT-1 (Lysosomal Associated Amino acid Transporter). We used this marker to visualize the subcellular localization pattern of lysosomes and to determine whether lysosomal localization changes in autophagy pathway component mutants. For future directions, we are also performing a forward genetic suppressor screen in one of the autophagy mutant backgrounds to determine other genes acting in this pathway to instruct presynaptic assembly.

"I don't want to live anymore": Analyzing depression-related content on Tumblr

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Depression among adolescents and young adults is a serious concern. Previous studies suggest that depression is a risk factor for self-harm and suicide. Further, suicide is the third leading cause of death among 10-24 year-olds. Social networking sites (SNS), such as Tumblr, are an important medium of communication for young people. Thus, SNS may be a useful way of understanding how young people communicate about mental health topics such as depression.

In the present study, we assessed the content of 17 of the *most popular* Tumblr accounts with a focus on depression, self-harm, and suicide. A total of 2,866 posts randomly selected from the 17 Tumblr accounts were analyzed and characterized for common themes. Using pictures (n = 1223, 42.6 %), text (n = 777, 27.1%), or a combination of pictures and text (n = 324, 11.3 %) to express feelings was common. Across all 17 Tumblr accounts, common themes were sex/issues with romantic relationships (n = 411, 14.3%), feeling alone (n = 402, 14.0%), self-loathing (n = 386, 13.5%), self-harm (n = 370, 12.9%), weight/body image issues (n = 333, 11.6%), and suicide (n = 294, 10.3%). The posts examined in the present study provide the public with a snapshot of the prevalence of depression-related content on Tumblr. Our findings underscore the use of Tumblr as an SNS where communication about depression, self-harm, and suicide occurs. We also emphasize an important need to uncover how posts correspond with actual mental illness.
Poster Presentations
The human respiratory tract is constantly exposed to dangerous microbes and pollutants. The immune system thus responds to protect the host. An imbalance in the immune system's inflammatory response in the airways can lead to mucus overproduction and subsequently result in acute and chronic respiratory diseases. Airway mucus overproduction is a prominent pathology in Chronic Obstructive Pulmonary Disease. Studies have shown that the mechanism responsible for mucus overproduction is triggered by the inflammatory interleukin (IL-13), which signals for the expression of the chloride channel calcium activated 1 (CLCA1) protein. Upon activation of this pathway, healthy cells of airways become goblet cells, whose function is to secrete mucin. Using qPCR, sequence alignment, and Immunoblotting, it was determined that CLCA1 has to undergo a self-cleavage which is required to create the active form of CLCA1 that can drive mucus overproduction and activate calcium-activated chloride channels. This makes the metalloprotease domain the "master regulator" of CLCA1 activity and also an ideal target for creating anti-mucus drugs. We hypothesize that CLCA1 undergoes its self-cleavage using a novel metalloprotease domain since its activities are not resisted by many commercially available and custom-made metalloprotease inhibitors. We currently have no structural data for any portion of CLCA1. To facilitate this, we have focused on expression, purification, and crystallization of CLCA1 constructs including the metalloprotease domain. Crystallization trials were conducted and the latest results will be shown. Ultimately, we will want to obtain a crystal structure of CLCA1, and get a better understanding of its metalloprotease domain.

Neurocysticercosis (NCC) is an infection of the central nervous system by cysts (larvae) of the cestode Taenia solium (Ts). Currently used antibody detection assays lack the ability to distinguish active infection from past infections or exposure in endemic regions. Antigen (Ag) detection assays can be utilized to detect active infections, assess worm burden, and assist in targeting individuals for treatment. A monoclonal antibody (MAb) based Ag detection assay, termed the B158-B60 Ag-ELISA has been used in epidemiologic studies and post-treatment burden assessment, but widespread use is limited by availability and cost. Our goal is to develop an Ag detection test for NCC comparable to the B158-B60 Antigen-ELISA that can be readily used in laboratories and the field. Twenty-two hybridomas raised against Ts cysts were screened for reactivity against Ts extracts by direct ELISAs. The most reactive of the MAbs (designated A7, an IgM isotype) was used to develop an antigen capture ELISA with column-purified A7 for capture and biotin-conjugated A7 for detection. The sensitivity of the ELISA was ≥10 ng/ml Ts Ags, with minimal crossreactivity against related cestodes. The A7 Ag capture ELISA is currently undergoing optimization for detection of Ts Ag in CSF and serum samples from individuals with NCC. Once validated with patient samples, we will test the utility of the ELISA for screening, for evaluation of the efficacy of anthelmintic treatment, and to determine the endpoints of treatment. Future research will aim to characterize the target antigens bound by the monoclonal via immunofluorescence and western blot analyses and to utilize the recently published parasite genome to identify the peptide target.
Endocrine disruptors can adversely affect hormonal and neurological functions. Examples of endocrine disruptors include several classes of pesticides such as chlorinated pesticides and nitrogen-containing pesticides. These pesticides have been heavily used in agriculture. Therefore, the purpose of this experiment is to measure the concentrations of endocrine disruptors in grocery-sold produce. This pilot study will provide baseline data on potential exposure to pesticide residues. The objectives were to qualitatively determine if the five produce apples, kale, cucumber, strawberries and blueberries contained pesticide residues. Methods were nutrient content analysis, homogenization, extraction, solvent exchange and Gas Chromatography- Mass spectrometry test. Based off the results of the GC-MS, there were a variety of pesticides found on each of the tested produce. There were also several unidentified peaks which may indicate more pesticides not mentioned in this study. In conclusion there is a need to monitor pesticide residues in local produce.

Prostate Cancer is a multifocal disease having cells with varying sensitivity to anti-hormone therapy. An effective initial treatment for prostate cancer patients involves androgen deprivation therapy. Investigators have demonstrated that androgen withdrawal can be a classical stimulator of neuroendocrine (NE) cell differentiation within a certain population of prostate cells. Whereas normal prostate tissue contains a very low number of neuroendocrine cells, the cancerous prostate gland tends to harbor a higher percentage of differentiated NE cells, the function of which is uncertain. To gain insight into this phenomenon we first investigated whether our LNCaP cells have or could be induced to express a NE phenotype. We compared the immunohistochemical profile of LNCaP under conditions that mimic therapeutic androgen ablation vs. prostate cancer cells grown in the presence of environmental androgen. After having established the baseline response, we then investigated whether the polyphenol Dibenzoylmethane (DBM), an LNCaP growth inhibitor, affected these cells ability to differentiate along a neuroendocrine pathway in the presence or absence of exogenous. Because data suggests that NE differentiated cancer cells are capable of secreting neuropeptides and cytokines, we sought to address whether DBM might mitigate LNCaP growth by affecting a paracrine feedback mechanism.
Characterization of a Highly Stable Esterase from Hypersaline Environment

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Background: Esterases are used as biocatalysts for the hydrolytic resolution of important pharmaceutical intermediates with excellent chemo-, regio-, and stereo-selectivity. With the aim of finding new esterases highly stable in a broad range of organic solvents, 148 halophilic microorganisms from the salterns of Cabo Rojo (Puerto Rico) were cultivated in marine broth, and screened for esterase activity using p-nitrophenyl acetate as chromogenic substrate.

Results: Microorganisms positive for esterase were tested for activity and stability after 24 hours of incubation in a broad range of organic solvent/water mixtures at different ratios (15%, 30% and 50% (v/v)). A new halophilic esterase (MO-12) closely related to Bacillus subtilis was selected as the most promising enzyme for biotechnological application. The enzyme was characterized in terms of stability to organic solvents, optimum salt concentration, pH and temperature. Methods: The crude enzymatic preparation was precipitated with ammonium sulphate, and after dialysis and lyophilization it was purified using SDS-PAGE. The esterase band was excised from the gel, eluted, and analyzed through mass spectroscopy. Conclusion: MOS 12 esterase is active and stable at high temperature (thermophilic properties). pH 9.5 is the greatest pH for the esterase activity. Potassium ions are more favorable than sodium ions for the enzymatic action. Acknowledgements: This project was supported by the NIH-MARC program at the University of Puerto Rico-Humacao.

Microsecond Simulations of MDM2 and its Complex with p53 Yield Insight into Force Field Accuracy and Conformational Dynamics

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There currently exists a large number of molecular mechanics force fields for protein systems, with many recent parameterizations designed to make improved predictions of NMR observables. Here, we present a systematic comparison of nine popular force fields (AMBER ff03, ff12sb, ff14sb, ff99sb, ff99sb-ildn, ff99sb-ildn-nmr, ff99sb-ildn-phi, CHARMM22*, and CHARMM36) in explicit-solvent simulations of native-state MDM2 and its complex with p53, over trajectory lengths as long as one microsecond. We find similar performance across all force fields in predicting rmsd fluctuations from the native structure and chemical shift predictions, with CHARMM22* and ff14sb potentials giving slightly better performance. Our results suggest that for this system, newer force fields are indeed more predictive than earlier parameterizations, information that can help guide future computational predictions of folding and binding properties of MDM2 and its ligands. Additionally, we present ongoing work in modeling the binding pathways of the p53 peptide to MDM2 and modeling the folding of the N-terminal MDM2 “lid” region, which limits ligand binding, using markov state modeling approaches.
### Biochemistry

**Label-Free Quantitative Proteomics Identify Global Protein Interactors for the Androgen Receptor Associated Cochaperone SGTA**

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Molecular chaperones facilitate proper folding and regulation of steroid hormone receptors (SHRs). Upon proper folding, SHRs bind ligand with high affinity, translocate to the nucleus and initiate gene expression accordingly. A novel cochaperone, human small glutamine rich TPR (tetratricopeptide repeat) containing protein alpha (SGTA), is a down-regulator of androgen (AR), glucocorticoid (GR), and progesterone (PR) receptors. It binds to heat shock protein (Hsp) 70 and 90 kDa. Additionally, SGTA plays a role in cellular processes such as cell cycle progression and apoptosis. Therefore, label-free quantitative proteomics was utilized to determine novel interactors in LNCaP human prostate cancer cells. Unknown protein interactions were purified using a Nickel resin and further analyzed with liquid chromatography mass spectrometry (LC-MS/MS). To determine if interactions were transient or strong, a comparison of a 3-hour versus an overnight incubation was used. Preliminary studies using rigorous statistical analysis have identified a broad range of proteins involved in different pathways other than the chaperoning pathway. Thus, future studies aim to validate these interactions with SGTA using nickel purification and assess their functional relevance, which will contribute to the understanding of the role SGTA plays within the chaperoning pathway and any cross-talk with other pathways.

### Biochemistry

**Development and Mechanism Study of Novel Imine-induce Hydroxyproline Ligation Methodology**

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The development of chemoselective ligation represents a major interest in synthetic peptide chemistry. The first major breakthrough began with the discovery of native chemical ligation, which employed cysteine's bifunctionality to realize a native peptide bond chemoselectively. During the last two decades, major research efforts have been focused on applying this approach to other amino acid sites of ligation. Proline reacts at the slowest rate of all natural amino acids in chemical ligations, owing surprisingly not to steric effects but rather non-covalent electronic effects of the unique orientation of amide carbonyls in Xaa-Pro peptidic linkages.

To address this problem of proline-site ligation, we developed a hydroxyproline ligation strategy, based on native chemical ligation "capture-rearrangement" principles, utilizing hydroxyproline's chemoselective bifunctionality. An auxiliary salicylaldehyde is first installed on the C-terminus of one peptide. This furnishes an electrophilic aldehyde for the N-terminus to attack forming a iminium via a Schiff's base-type mechanism. Once the second peptide is captured, a first rearrangement is undertaken in which the hydroxyl group at the 4 positions attacks the iminium, forming an aminal. The nitrogen is then free to undergo the second rearrangement where the nitrogen attacks the carbonyl of the C-terminus and establishing the native peptide links. We successfully demonstrated on an array of fully characterized oligopeptide systems that this approach achieves ligation at difficult proline sites in a generalizable fashion. Additionally, we studied the mechanism of hydroxyproline-site ligation to further understand this reaction. We successfully isolated the key bridged bicyclic aminal intermediate which verifies the proposed mechanism.
Ovarian cancer is a deadly gynecological disease. Hyperthermia has been investigated as potential treatment for cancerous tumors. However, its localized application still remains a challenge. Magnetic fluid hyperthermia (MFH) is an alternative to surpass this challenge. To understand the underlying molecular mechanisms of MFH a gene expression study was performed in ovarian cancer HeyA8 cells line. Analysis revealed that heat shock protein genes including HSPA6 were upregulated when treatment was applied at 43°C for 30 min. HSPA6 encodes the heat shock protein HSP70. HSP70 gene expression was confirmed by PCR in HeyA8 and A2780cp20 cell lines at 39, 41 and 43°C and at 1 hour after treatment was observed the highest expression. The effects of HSP70 inhibition in ovarian cancer cell lines during magnetic fluid hyperthermia application were investigated. The hypothesis states that the inhibition of HSP70 will decreases cell viability when MFH is applied to cancer cells. si-RNA inhibition of HSPA6 gene was achieved in vitro and a decrease in cell viability was observed when cells were exposed to MFH. An alternative avenue of inhibition was examined by using a small HSP70 inhibitor known as 2-phenylethynesulfonamide (PES). An improvement in MFH efficacy was observed in various cell lines (A2780cp20, SKOV3 and HeyA8). Combination index was calculated reporting a synergistic effect. In vivo efficacy experiments were also performed in Nu/Nu mice with HeyA8 a subcutaneous tumor model. A reduction of tumor growth was observed. HSP70 inhibition is a promising target to improve MFH and become a cancer new therapy.

Collagen is the primary building block for many biological tissues including bone, muscle, cartilage and skin. Type I collagen is also the most important structural element of the extracellular matrix. In animals, collagen fibers transmit forces, dissipate energy, and prevent mechanical failure in normal tissues. Although it is an essential part of the human and animal bodies, the mechanical properties of Type I collagen have not been adequately quantified due to the diverse structures and purposes it serves. In the present study, collagen fascicles that were extracted from the tail tendons of male Sprague-Dawley rats were tested in a MiniMat tensile tester at varying strain rates. The fascicles were previously submerged in a calcium phosphate solution to induce tissue mineralization. The fascicles were maintained in a wet state during testing. Initial results show that at deformation rates of 2.5 mm/s and 10 mm/s, no significant changes in the modulus of elasticity were observed. However, the elongation to failure decreased at the higher deformation rate. Mineralized fascicles showed an increase in the Modulus of Elasticity while showing a decreased percentage of elongation as expected. Further tests are being carried out to characterize the mechanical behavior of the fascicles under monotonic and cyclic loading conditions.
While the clinical benefits of a chest computed tomography (CT) exam generally outweigh the risk of radiation exposure, the scientific and clinical community has more recently focused on cumulative radiation and its potential health risks. The breast and lung tissue is the most radiosensitive tissue within the scan region of a chest CT exam. Standard effective dose estimates using k-factors do not account for patient-specific factors such as body habitus or patient-specific anatomy. Patient-specific dose maps can be used to estimate radiation dose to breast and lung tissue during cardiovascular CT exams and demonstrate the variability of breast and lung dose among these patients. Insight gained from patient-specific dose maps may lead to better CT dose management.

Autophagy is a survival mechanism utilized by all eukaryotic cells during nutrient starvation in which the cell recycles proteins and other cytoplasmic components to the vacuole to degrade and release. Understanding this mechanism can potentially improve cell survival after stroke and heart attack, thus minimizing tissue damage. Macroautophagy, the better known autophagy pathway, involves recycling cellular components via a double-membrane bound vesicle, whereas microautophagy is poorly understood and involves the vacuole directly engulfing the cytoplasmic components. Previous internal studies showed glucose starvation inhibited macroautophagy in S. cerevisiae (budding yeast) cells; however, some autophagic activity was still detected by an alternate quantitative assay. To determine whether this activity was due to microautophagy, we investigated the consequences of deleting a critical gene for macroautophagy, Atg5, and genes that potentially influence microautophagy, Vtc1 and Vtc2, in a Pho8Delta60 strain, allowing us to measure autophagy quantitatively through the Pho8Delta60 enzymatic assay. We starved these strains for nitrogen, glucose, or both nitrogen and glucose for ~30 hours and found that Vtc2, not Vtc1 or Atg5, was required for autophagic activity in glucose-starved cells. We concluded that microautophagy occurs in glucose-starved cells, and some of the genes in the vacuolar transporter chaperone (VTC) complex are more important for microautophagy in glucose-starved cells than others. In the future, we plan to measure lipid droplet autophagy using a biosensor assay that we are currently optimizing to measure bulk autophagy.
Confirming the Deletion of Proteins Relative to Adaptation in Response to Small Bowel Resection

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Short bowel syndrome (SBS) is a condition in which nutrients are not properly absorbed due to small bowel resection (SBR). Following SBR, a normal physiological process known as intestinal adaptation is expected to occur and result in intestinal morphology changes increasing functional capacity. Previously, both enterocyte specific epidermal growth factor receptor (EGFR) and insulin like growth factor 1 receptor (IGF1R) were independently proven to be unnecessary for normal adaptation. The purpose of this study was to evaluate the concurring effects of deleting both EGFR and IGF1R in the intestine. A tamoxifen inducible Villin-Cre recombinant system was used to generate double knockout mice. Enterocyte specific EGFR and IGF1R double knockout mice (EGFR/IGF1R-IKO) (n=6) and their wild-type (WT) underwent 50% SBR. The mice were harvested in order to isolate the small intestine enterocytes and smooth muscle needed to score structural adaptation and measure cell proliferation and apoptosis. Protein quantification was used to determine concentrations necessary for western blotting. The knockout of both EGFR and IGF1R were confirmed. After 50% SBR, EGFR/IGF1R-IKO mice and their WT displayed normal adaptation. No significant difference in rates of proliferation and apoptosis were present between WT and KO mice. Submucosal capillary density following SBR increased in WT but not in EGFR/IGF1R-IKO mice. Disturbing EGFR and IGFFR expression in the intestines does not alter resection-induced structural adaptation following SBR. The findings from this study suggest that villus growth is directed by pathways and receptors located outside of the epithelial cell component in the small bowel.

Morphological Plasticity and Gene Expression Plasticity are Significantly Correlated

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The budding yeast Saccharomyces cerevisiae is a model for cellular aging. Yeast aging is often measured by its replicative life span or (RLS), which is determined by the number of cell divisions that occur prior to senescence (when cells can no longer divide). We recently showed that cellular aging is an emergent property of gene networks and the aging dynamics are influenced by network robustness. Here, we studied the role of robustness on replicative aging in S. cerevisiae. As a cell’s network robustness decreases, it will be less able to adapt against external perturbations. Several measures of robustness measure are examined, including morphological robustness, network connectivities, growth fitness and gene expression plasticities. Our studies show that the yeast replicative aging correlates with these robustness measures.
The expression of human vascular adhesion protein-1 (hVAP-1) is induced at sites of inflammation where extravasation of lymphocytes from blood to the peripheral tissue occurs. The X-ray structure of hVAP-1 has shown many features related to specific function. Recently, evolutionary RNA phage display was used to evolve epitopes. We used the RNA coliphage, Qbeta to investigate structure related to the function of hVAP. To achieve this, a 308 bp DNA portion of the hVAP protein and 8 histidine genes were inserted into our plasmid bearing the entire genome of the Qbeta phage at the end of the A1 minor coat protein. The recombinant plasmid obtained produced phages (Qbeta-hVAP). The phage plaques were small in size compared to the wild type with a titer of 10^8 p.f.u/ml. Qbeta-hVAP phages showed DNA band size of hVAP after RT-PCR. The presence of hVAP within the cDNA of Qbeta was confirmed by dot blotting with the 8His-Tag antibody. The position of hVAP on the exterior surface was confirmed by electron microscopy with NTA-Gold. Successfully, hVAP was displayed on the exterior surface of the RNA phage. This is the first study showing a peptide, other than an epitope, can be presented on the surface of an RNA phage. We are planning to randomize the portion close to the RDG motif of hVAP and to study the kinetics of binding and functional properties of the library. Also, novel function can be gained from the same library. Results obtained can be extended to proteins from the same family.

Vascular smooth muscle cells (VSMC) comprise the medial layer of the blood vessel wall. These cells are necessary for the regulation of blood pressure and are able to do so by contracting and relaxing to alter the luminal diameter arteries and veins. This constant contraction and relaxation is created by stress fibers and provides continuous maintenance of blood pressure. Stress fibers are composed of actin molecules that have been cross-linked by cross-linking proteins. It has been found through co-localization and Co-immunoprecipitation (Co-IP) experiments in human embryonic kidney (HEK) cells that the A2b Adenosine Receptor (A2bAR) is a novel binding partner of an actin cross-linking protein. Therefore, we hypothesized that stress fiber formation is regulated through the A2b Adenosine Receptor. This receptor is one of four G-protein coupled receptors of the vasodilator adenosine. The four receptors are A1 and A3, which are inhibitory receptors for cyclic adenosine monophosphate (cAMP), and A2a and A2b, which serve as stimulatory receptors for cAMP. To test this theory, stress fibers were visualized in VSMCs using immunofluorescence after either knock-down of the A2bAR or cytochalasin D wash out with BAY stimulation. We found that changes in stress fiber formation after knock-down of A2bAR or wash out of cytochalasin D with BAY stimulation were not noticeably visible. Future research may include cytochalasin D washout of knock-down A2bAR VSMCs as well as VSMCs overexpressing A2bAR to determine the role of the A2bAR in the formation of stress fibers.
Saccharomyces cerevisiae (SC), commonly known as baker’s yeast, is a eukaryotic organism that has the ability to produce haploid germ cells through the process of meiosis. SC is a beneficial biological model because of its short generation time, and its ability to be easily transformed. Previous studies have shown that bub3 knockout strains do not make it through meiosis in its entirety; Bub3 is one of 3 main spindle assembly checkpoints (SAC) proteins. However, exact location of meiotic arrest has yet to be determined, and it is hypothesized that Bub3 plays additional roles in the cause of this. The meiotic arrest point will be pinpointed by looking specifically at Zip1 and Rec8 which localize in prophase and S phase respectively. A series of transformation and PCR reactions were paired to knockout the BUB3 open reading frame (ORF) and replace them with Hygromycin B ORF. After transformation was successful, haploid cells were mated to form a bub3 homozygote in strains with Zip1-GFP or Rec8-GFP. The knockouts were verified by PCR. Fluorescence expression was measured to check percentage of cells expressing Zip1-GFP. The purpose of this experiment was to determine at which phase in the cell cycle meiosis is blocked in bub3 knockout cells. Our lab team has already shown that the cells enter meiosis based on the presence of the Ime1 marker, a transcription factor that is turned on as cells enter meiosis. In the event that cells express Zip1-a synaptonemal complex component, we can conclude entrance into meiotic prophase.

Sigma virus, a member of the Rhabidovirae family, is a vertically transmitted virus and known to induce carbon dioxide sensitivity in Drosophila Melanogaster. The main purpose of this study is to investigate the relationship between diet (specifically methionine), sigma infection and other life history traits on the fecundity of D. Melanogaster. Two hypotheses have been formulated regarding this relation. The first hypothesis deals with methionine acting as a stimulator of the insulin signaling pathway which in turn activates the antiviral response in D.melanogaster. Since methionine is an essential amino acid, the second hypothesis states that its presence in diet can induce longevity and higher fecundity. To test these hypotheses, we conducted two different kinds of studies: egg count and ovariole count. For egg count, we created a total of 80 vials consisting of combinations of two genotypes, two dietary conditions(with and without methionine) and two infection statuses(uninfected and infected). The female flies raised in those 8 combinations were then dissected and the number of ovarioles were recorded. Based on these studies, we were able to find out that the flies raised in the without methionine conditions had higher fecundity and higher ovariole count when infected with the virus. We also found significant relationships between the infection status and fecundity and between the diet/genotype combination and fecundity. This positive correlation favors the insulin signaling pathway hypothesis. In conclusion, we deduce that the methionine activates the insulin signaling pathway and generates an antiviral response in the host cells.
**Genetics**

**Characterization of H3.3 Histone Variant HIS-74 in the Germline of Caenorhabditis elegans**

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Histone proteins wrap DNA to form nucleosomes and compact eukaryotic chromosomes. Histones exist as variants that play significant roles in gene regulation and expression. Histone variant H3.3, which is structurally similar to histone H3, is associated with transcription. Three H3.3 histone variants (HIS-71, HIS-72 and HIS-74) have been identified in C. elegans but of these only HIS-71 and HIS-72 have been partially characterized. This study seeks to characterize the role and function of HIS-74, an H3.3 variant that differs from the other H3.3 variants. A GFP-tagged HIS-74 transgene demonstrates germline-specific expression with differences in its stability within the genome between sperm and oocytes. A strain carrying a deletion allele that removes both his-74 and an adjacent gene, ccch-3, exhibits embryonic lethality. RNA interference (RNAi) of the ccch-3 gene alone exhibits no significant lethality, indicating that deletion of the ccch-3 gene is not responsible for the lethal phenotype in the strain. Mapping and outcrossing experiments could not separate the lethality from the deletion, further implicating the loss of his-74 in the lethality. However, a mutation with a premature stop codon in his-74 has no phenotype and we have not yet been able to rescue the mutant strain with a transgene covering the deletion. A his-74/- knockout line is currently being generated using CRISPR/Cas9 technology. Further studies will seek to better understand the HIS-74 function and interplay with the other two H3.3 histone variants HIS-71 and HIS-72.

**Genetics**

**Evaluation of Pediatric Sickle Cell Pulmonary Function Complications**

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Our purpose is to improve pediatric sickle cell child health by means of preventative bronchodilator therapy. It is likely that with appropriate intervention and bronchodilator therapy, pediatric sickle cell child health will improve, decreasing the number of hospitalizations and emergency room visits. Data was extracted from medical chart reviews, pulmonary function tests, echocardiograms to identify any cases of pulmonary hypertension, and a questionnaire to identify any complications of asthma. Approximately 3 out of 4 patients (72%) at Children’s Hospital of New Orleans exhibited Pulmonary Function Test results indicative of asthma, but had not been given the diagnosis of asthma or received treatment for asthma. 76.36% of the patients that had 3 or more hospitalizations/ER visits belonged to the HgbSS patient demographic. Also, the HgbSS patients had substantially lower DLCO in comparison to the other patients (p=0.02 vs. HgbSB-thal), (p=0.04 vs. HgbSC). HgbSS patients encounter more health complications. In this study, pediatric sickle cell patients have proven to be under-diagnosed for asthma and other pulmonary disorders. HgbSS patients encounter more health complications and more frequent hospitalizations and Emergency Room visits in response to untreated pulmonary function complications. In the future, we plan to assess PFT data and overall health pre-bronchodilator treatment and post-bronchodilator treatment to identify improvements. Further research includes mimicking the processes of the least volatile patient populations to render healthier pediatric sickle cell patients through bronchodilator therapy, but the ultimate goal is to identify and treat all individuals with sickle cell disease, asthma, and other pulmonary function complications.
Mapping a Recessive Modifier Locus Which Suppresses a Dominant Spinocerebellar Ataxia Mutation in Mice

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We have identified and characterized a mutant mouse strain, BxR23, that exhibits a late-onset spinocerebellar ataxia (SCA) inherited as an incompletely dominant trait. Although the precise location of the mutation in BxR23 has not been identified, we have narrowed the location to a 1.2 Mbp segment on Chromosome 9. When BxR23 mice are intercrossed with mice from either of two strains (BALBc or CAST/Ei), the proportion of affected mice is significantly less than expected for an autosomal dominant trait. Furthermore, when the ataxia gene segment from BxR23 is backcrossed onto the BALBc background, the ataxia phenotype is completely masked in all N10 offspring. We hypothesize that a modifier gene, acting as a recessive suppressor, is located in the genome of BALBc and CAST/Ei. A genome-wide analysis of DNA markers in the F2 offspring of a BxR23 x CAST/Ei intercross identified three regions as a possible location for the modifier locus: Chromosome 1 (100 Mbp), Chromosome 9 (100 Mbp), and Chromosome 10 (100 Mbp). We are analyzing DNA markers within each of these regions, in 100 F2 offspring, to identify any correlation between a region and the modifier phenotype. Phenotypes (ataxic, normal, suppressed normal) for each of the 100 offspring have been determined. "Suppressed normal" mice are those with the ataxia mutation, but with a normal phenotype. These mice are hypothesized to be homozygous for the modifier; thus, a DNA marker exhibiting homozygosity for the CAST/Ei allele in suppressed normal mice would likely mark the position of the modifier.

Investigating the Effect of the Microbiome on Hematopoiesis

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We determined the effect of the microbiome on adult hematopoiesis as well as in the context of aging. 12 months and 3 months adult mice raised under germ-free and conventional housing conditions were used for this experiment. Bone marrow was isolated from the femur, tibia, and spine in order to determine the number and frequency of hematopoietic cells, including hematopoietic stem and progenitor cells and mature cells. Data collected included the complete blood count (CBC), total bone marrow counts, flow cytometric analysis of bone marrow hematopoietic stem and progenitor cells and mature cells, as well as peripheral blood mature lineages, and methylcellulose colony forming assays. Whereas the colony forming capacity of progenitor cells was significantly decreased in germ-free mice, the frequency of long-term hematopoietic stem cells (HSCs) was significantly increased, suggesting that the microbiome may negatively regulate expansion and/or differentiation of progenitor cells, but may positively regulate hematopoietic stem cell function. Not all hematopoietic cells that arise from HSCs are influenced by the microbiome, and the microbiome has selective positive effects on progenitors, and possible negative effects on HSCs, in both young and old mice. A common finding present in both young and old mice is that lymphoid cells are greatly dependent on the microbiome, and the germ-free environment promotes loss of lymphoid cells, which indicates that the microbiome exerts significant role in the production of immune cells in the bone marrow.
Recent studies have highlighted the ability of some bacteria to utilize fatty acids as a membrane remodeling strategy. Considering this, we hypothesized that fatty acid-containing cosmetic products, such as lotions, may have an effect on skin-dwelling bacteria. The current study surveyed Acinetobacter baumannii for its growth under skin conditions (minimal media, pH 5.5, 150 mM NaCl, 30 degrees Celsius) and membrane lipid response to fatty acids found in daily-moisturizing lotions. Since phospholipid profiles from A. baumannii suggested structural changes, a crystal violet (CV) uptake experiment was performed to assess bacterial uptake of hydrophobic compounds, a key indicator of membrane permeability. Differences of up to 20% CV uptake were observed, demonstrating decreased membrane permeability to hydrophobic compounds following lotion fatty acid exposure. A. baumannii phospholipids were then extracted following growth in the presence and absence of lotion fatty acids and analyzed by high-performance liquid chromatography/mass spectrometry (HPLC/MS) to confirm bacterial synthesis of phospholipids possessing acyl chains corresponding to the supplied fatty acids. The ramifications of fatty acid utilization were explored by performing acid and salt stress assays on A. baumannii following growth with lotion fatty acids. Although minimum inhibitory concentrations were unaffected, the fatty acid treated bacteria exhibited variable growth effects upon exposure to increasing concentrations of sodium chloride and lactic acid.

Ongoing experiments are examining biofilm formation and whether fatty acids affect bacterial survival after exposure to antimicrobial peptides and other environmental stresses.

Heavy metal pollution due to legacy waste from the Cold War nuclear proliferation remains a huge problem at federal and industrial sites. Microbial bioremediation is a cost effective method for removing heavy metals from soil and groundwater. The purpose of this study was to characterize the growth pattern of a Serratia marcescens strain 93-1399-1 in the presence of the heavy metal hexavalent chromium (Cr [VI]) and its ability to convert Cr (VI) to the less toxic Cr (III). When S. marcescens was grown on LB agar with increasing concentrations of Cr (VI) as potassium dichromate, the bacteria survived at all concentrations tested up to 200 ppm. Growth curves of S. marcescens in Cr (VI) showed that the bacteria exposed to 25 ppm grew in similarly to bacteria without Cr (VI), had reduced exponential growth at 50 and 100 ppm and poor growth in 200 ppm after 24 hours. Plate count assays showed that the 65% of the bacteria survived in 25 ppm of Cr (VI) but on only 5% survived at 50 ppm. In preliminary chromium reduction assays, S. marcescens was grown for 24 hours in 25 ppm of Cr (VI). S. marcescens reduced 60% of the Cr (VI) to Cr (III) as compared to 4% reduction in broth alone. These data suggest that the S. marcescens strain may be useful in bioremediating Cr (VI) at contaminated sites. Future studies will focus on identifying the genes responsible for Cr (VI) reduction.
Herpes Simplex Virus type one (HSV-1) is a double-stranded DNA virus belonging to the Herpesviridae family. It is estimated that over 60% of the United States population is infected with HSV-1 (Xu et al, 2006) and it is continually documented as a leading infectious cause of corneal blindness and encephalitis (Webre et al, 2011). After initially infecting epithelial cells, HSV-1 virions travel to sensory ganglia neurons where they form a latent infection and remain until reactivation. The Renin-Angiotensin System (RAS) is a hormonal cascade functioning primarily to maintain homeostatic control of arterial and osmotic pressure. In addition to its well-known function, research suggests RAS components such as Angiotensin peptides may have some concentration dependent anti-viral effects in H1HeLa cells (Ang et al, 2012). Losartan, an angiotensin II receptor antagonist, has been shown to have protective effects in a murine viral myocarditis models caused by coxsackievirus B3 (Zhang et al, 2013). Thus, we tested the hypothesis that Captopril attenuates cytopathic effects of HSV-1 in SH-SY5Y neuroblastoma cells. Preliminary data, via cell viability utilizing trypan blue (p-value=.011) and a MTT assay illustrating a dose-dependent increase maxing out at 1nM concentration, suggests Captopril offers some mechanism of protection, making cells less susceptible to cell death caused by HSV-1 infection. The ability to better understand mechanisms affecting infection and reactivation may provide insight into valuable therapeutic alternatives possibly capable of preventing infection or reactivation. Based off experimental results, Captopril and components of the RAS may prove to be effective therapeutic targets in HSV-1 infection.

Little is known regarding the nature and function of the myosin motors of Plasmodium. Analysis of the genome reveals that there are six myosin heavy chains but only the role of Myosin A, along with its cognate light chain partner, Myosin A Tail Interacting Protein (MTIP), has been well characterized in the process of parasite invasion. PFF1320c is annotated in the Plasmodium genome as a putative myosin light chain but to date there is no biochemical evidence to support this designation. Preliminary studies of PFF1320c have shown that the protein is essential due to our inability to disrupt the gene. Expression of a tagged version of the gene at an ectopic site permitted a successful knockout of PFF1320c. Size exclusion chromatography suggests the protein is assembled in a high molecular weight complex, indicative of formation of a myosin motor. Studies are currently underway to identify the myosin heavy chain (MHC) partner by co-localization of co-transfected tagged versions of four of the six MHC and PFF1320c, utilizing immunofluorescence assays. We hope to identify potential binding partners of PFF1320 through proximal biotinylation using the promiscuous biotin ligase BirA. We are also working to phenotypically characterize the role of this presumptive actin myosin motor within the parasite using the glmS-Ribozyme as an alternate knockdown strategy. Further characterization of this presumptive myosin light chain and identification of the MHC partner will provide an insight into the role of this unique myosin motor in the growth and development of the parasite.
Diatoms are a group of unicellular algae enclosed in a siliceous exoskeleton called the frustule. This ornamented structure allows for taxonomic identification. Diatoms are frequently used as indicators to monitor the integrity of aquatic ecosystems in Europe, Africa and the United States. This study aims to expand the knowledge of these microalgae for the future inclusion of diatom monitoring as part of trophic status monitoring in Puerto Rican Reservoirs. Net-size plankton was sampled from six reservoirs, Cerrillos, Cidra, Guajataca, La Plata, Patillas and Toa Vaca, which were selected to encompass a wide range of trophic status, oligotrophic to eutrophic. A total of 6 samples were collected from each reservoir, collection dates ranged between March 2012 and April 2014. Samples were analyzed with light and SEM-microscopies and identified to the lowest taxonomic rank possible. Diversity (Shannon-Weaver’s, H’), richness (Margalef’s, R), similarity (Jaccard) and Pollution Tolerance Index were calculated. A total of 32 taxa were identified. Dominant taxa in these reservoirs were species of Achnanthidium, centric diatoms, Navicula and Ulnaria. Mesotrophic reservoirs (Guajataca and Toa Vaca) had the most diverse communities and the highest richness. Some organisms present in the phytoplankton communities, such as Achnanthidium minutissimum and Ulnaria ulna, could aid in the differentiation of low nutrient states from high nutrient states. The study showed that phytoplankton taxa seem to be useful in the bioindication of the trophic conditions in subtropical reservoirs.

Introduction: Antibiotic resistance is a major concern in public health. One common drug-resistant pathogen is Acinetobacter baumannii. 3 out of 5 people infected with A. baumannii will bear a strain that is highly resistant to antibiotic treatments. An important class of antibiotics that has lost its efficacy against A. baumannii is the fluoroquinolones. One possible strategy to address the antibiotic resistance problem is to recover the efficacy of fluoroquinolones by inactivating or limiting the bacterial resistance mechanisms.

Hypothesis: We hypothesize that there are genes in A. baumannii that, when inactivated, increase the susceptibility of the bacterium to fluoroquinolones. Moreover, we believe that there are genes with an important but undetermined role in ciprofloxacin resistance.

Methods: We used Tn-seq, a high-throughput genomics approach, to identify genes that enhance the effects of ciprofloxacin, a prototypical fluoroquinolone. We have also isolated ciprofloxacin-resistant isolates, and characterized them by whole genome sequencing. The minimal inhibitory concentrations, as well as other relevant characteristics were assessed. Results: Our preliminary hits underlined the importance of specific functions for A. baumannii to resist ciprofloxacin. Importantly, we have identified genes not previously implicated in ciprofloxacin resistance in vitro. Interestingly, no significant fitness defect was seen due to these mutations. Conclusion: We have preliminarily identified functions that are of importance for A. baumannii to resist fluoroquinolone antibiotics, such as ciprofloxacin. This phenotypic screening has provided important insight into how A. baumannii can intrinsically resist fluoroquinolones and, more importantly, what alternate functions could possibly be targeted to improve fluoroquinolone therapies.
The ability of a forager to gain information about its surrounding environment may influence its decision of where and how long to forage (Brown 1988, Valone and Giraldeau 1993). Typically eastern chipmunks, Tamias striatus, eavesdrop on the alarm calls of birds in the Paridae family such as eastern tufted titmice Baeolophus bicolor and black capped chickadees Poecile atricapillus to gather information about the cost of predation in the surrounding area. Since chipmunks vary their time spent foraging in relation to perceived foraging costs, the giving-up density (GUD) or the amount of food left over when the chipmunk decides to stop foraging is an indication of the animal’s patch use behavior and perception of predation risk. The purpose of this research is to measure giving-up densities (GUDs) of chipmunks in the presence of different alarm calls with and without background road noise to quantify the consequential changes in perceived predation risk. If road noise masks sounds in the environment, including alarm calls, chipmunks may have elevated predation risk. Chipmunks that perceive a greater risk from road noise increase vigilance and cease risky behavior faster as a result, leaving more food behind and yielding a greater giving-up density. Our results indicate that road noise can interfere with the chipmunk’s eavesdropping systems and consequently affect their cost-benefit analysis of foraging.

Alterations in temperature and precipitation as a result of climate change affect plant growth and productivity. Chronic drought events can have detrimental consequences on above- and belowground productivity. Belowground production, in particular, is critical for carbon storage, soil quality, and other ecosystems services. We investigated the impact of drought and changes in precipitation seasonality on belowground production in two desert grassland types in central New Mexico: shortgrass steppe dominated by blue grama (Bouteloua gracilis) and Chihuahuan Desert grassland dominated by black grama (B. eriopoda). Measurements were conducted in the Extreme Drought in Grassland Experiment (EDGE), which includes two rainfall treatments (66% rainfall reduction and a six week delay in monsoon seasonality) plus ambient plots. A total of 150 samples were collected from root ingrowth bags and measured for root biomass in five replicates of each treatment in each grassland type. Root ingrowth bags were buried to 15 cm pre-monsoon, and were extracted periodically during the growing season. An additional 58 bucket auger samples were collected pre-monsoon to determine belowground standing crop. We used ANOVA to determine if differences occurred in belowground standing crop and root production among the treatments at each site. Root production was highest in ambient plots (47.4 ± 15.4 g m^-2) and lowest in the drought treatment (11.3 ± 5.21 g m^-2) with intermediate values for the delayed monsoon season (29.6 ± 9.0 g m^-2). Our results demonstrate that chronic drought detrimental impacts on belowground production and that only partial recovery occurred in the delayed monsoon treatment.
Plants subjected to herbivory tend to suffer from reductions in fitness. Herbivory may also delay reproduction, which can negatively affect certain life history traits. Deer are overabundant and dramatically affect herbaceous plants through herbivory, possibly leading to selection for tolerance. This research investigated potential evolutionary responses to variation in herbivory. Specifically, it used the model organism American Bellflower \(C.\) \(americanum\) to investigate whether plants have evolved to tolerate deer herbivory and if tolerance varies among populations. Delays in reproduction associated with herbivory among populations were compared to determine if this could result in observed life history schedules. We evaluated whether the differences in phenology between populations contribute to response to herbivory by using three clipping treatments 1) plants clipped at the same calendar date, 2) plants clipped at a similar phenological stage, and 3) controls (unclipped). Additional plants open to natural deer herbivory were also observed and the fitness components of these plants were compared to those kept from natural herbivory. Population variation in tolerance to herbivory was determined by measuring vegetative growth and reproductive fitness components. This research project took place in Michigan and Georgia to allow the role of growing season on tolerance to deer herbivory to be evaluated. Knowledge of the association between deer herbivory and \(C.\) \(americanum\) performance and reproductive phenology will directly inform understanding of evolutionary responses to herbivory. The research will determine if tolerance to herbivory and delays in reproductive phenology following herbivory vary among populations and if this difference depends on the environment.

Diabetes increases the risk of breast cancer and breast cancer mortality, thus adequate breast cancer screening in older women with this condition is important. Moreover, because diabetes affects up to 18% of women 65 years and older, a significant relationship between diabetes and cognitive impairment would have important clinical and public health implications. Also, diabetic as well as pre-diabetic older women have impaired cognitive performance and are at greater risk for developing cognitive impairment. To fill a gap in the literature, we compared diabetic older women to healthy older women on: desire to improve their health, receiving mammograms and regular health screenings, as well as cognitive functioning. Participants \(n=72,\) Mean age= 69.29, SD = 6.579, age range=50-90 were multiethnic, non-institutionalized older women residing in Los Angeles County who completed our research packet. The latter contained the last author’s a) Demographics List and b) Older Women’s Health - Qualitative Protocol, as well as the well-known MiniCog (Borson, 2000). Results of an ANOVA and two Chi-square analyses showed that, as hypothesized, diabetic women desired to improve their health more than the women in the control group \(F(1,70)=11.87, \ p<.05, \ n\ square = .15\). Diabetes respondents were also significantly more likely to receive mammograms \(X^2(1)=5.87, \ p<.05\) and general health screenings \(X^2(1)=4.51, \ p<.05\). Surprisingly, in contrast with prior literature’s findings, cognitive health in the diabetic group obtained marginal significance in an ANOVA as being better than the cognitive health of the control group \(F(1,68)=3.30, \ p<.05, \ n\ square = .05\).
Women currently make up only 25 percent of the STEM workforce (NSF, 2013). Spatial skills have become a focus of interventions and preventive measures to lessen this disparity. Previous research highlighted spatial skills as malleable and predictive of STEM achievement (Newcombe, 2013), yet little examined the role of cultural factors, specifically, stereotypes. Research has demonstrated awareness of math-gender stereotypes as early as second grade with children exhibiting the cultural stereotype that boys are better at math (Cvencek et al., 2011). However, little research has examined spatial stereotypes, although studies indicate that they exist in adults (Fennema & Leder, 1990). The present study examined whether children exhibited gender-stereotyped preferences for spatial abilities. Three-, four- and five-year old participants (N = 91) were given a preference task in which they chose which novel characters were best at various spatial tasks. In each trial participants were told that one of the two characters (one male, one female) “was really good” at a specific spatial task and were asked to identify which character was better at the task or say they were the same. Three-year olds gave egocentric responses, displaying a preference for their own gender. By age five, both genders displayed a preference for males as better. This significant age by gender interaction (p = .028) supports the hypothesis that as children develop, so does their implicit awareness of spatial-gender stereotypes. This evidence of spatial-gender stereotypes by age five suggests that future research should examine possible interventions and factors influencing children’s implicit biases.

Background: In Puerto Rico (PR), cancer is the leading cause of death. Previous research has identified the need for cancer prevention education in PR. Cancer 101 is an educational resource designed to improve cancer education, reporting increased knowledge and attitudes. Although available in Spanish, we sought to identify if the curriculum needed cultural adaptation for the population in PR, which has a strong sense of identity influenced by acculturation and cultural nationalism. The purpose of this study was to culturally adapt the Spanish version of Cancer 101 for the PR audience. Methods: A local expert panel (n=6) collaboratively reviewed the curriculum for content, legibility, utility, and colloquialisms. Cognitive debriefing sessions were then held with 10 Master of Public Health (MPH) students to assess the adaptation’s strengths and weaknesses. Verbatim transcripts were created and a content analysis conducted to assess comprehensibility, utility, and satisfaction. Results: Panelists suggested adaptations included incorporating PR references/resources, updating objectives/evaluation items, and replacing words. Cognitive debriefing session participants were satisfied with the overall adaptation, in the areas of comprehensibility of covered topics; ease of use; and appropriateness of resources. Suggested edits included better tailoring the accompanying presentations to the PR community. Discussion: The two-phase curriculum review identified specific changes to content and cultural translation components, ensuring the adaptation is culturally and literacy-level appropriate and represents PR’s social context. Findings highlight the importance of further adapting Spanish educational materials across Hispanic sub-ethnicities. Next steps included developing a Cancer 101 training program to deliver cancer education in PR.
The present study examined gender differences in the behavior of children diagnosed with Sickle Cell Disease (SCD) with the occurrence of stroke and no stroke. The study utilized a between-subject experimental design with 55, African American participants, ages 4-18 years who have and have not experienced either a silent or overt stroke (15- stroke, 40- no stroke). The Behavioral Assessment System for Children (BASC) was administered to measure children’s behavior patterns on a series of clinical subscales and global composite scales. An independent sample t-test was conducted comparing four clinical subscales of males and females with and without stroke. Another independent sample t-test was conducted, comparing three global composite behavioral scores of SCD males and females with stroke and without stroke. Results yielded no significant differences (with a p <.05) in both sample t-tests between SCD children with and without stroke. A chi-square analysis showed children in the stroke group had higher percentages of individuals categorized as At-Risk for behavior problems, than children in the no-stroke group with SCD. The present study helped provide knowledge about behavioral trends stemming from stroke caused by SCD and how they relate to Conduct Disorder (CD). Proposed explanations for no differences between groups, in light of statistical trends, includes having a small sample size of the stroke group and the use of cross-sectional data. Future research may look to increase sample size and extend the current study longitudinally in order to measure behavior over time and perhaps find significant differences between groups.

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder marked by impaired social interaction/communication along with stereotyped/repetitive play. There is a pressing need for interventions that increase social interactions with typically developing (TD) peers. The goal of this study is to evaluate whether a shared interest in robotics was more prevalent in conversations between autism spectrum disorder (ASD) adolescents and typically developing (TD) peers after a weeklong robotics summer camp. Eight individuals with ASD and eight TD peers ages 12-17 participated in a weeklong robotics camp, during which they learned robotic facts, actively programmed an interactive robot, and learned “career” skills. Before and after camp, each pair of participants was asked to interact for 10 minutes. The room had several robot-related items along with other games, toys, magazines, and snacks. They were instructed to get to know each other. We evaluated pre- and post-camp interaction sessions and calculated: the number of times the word “robotics” or “robots” was said between the participants as they conversed with one another, and the number of times the two participants interacted with any of the robotics items in the room. Participants with ASD had a small increase from pre- to post- in the number of social interactions in which robotics was the shared topic of their conversation. Our findings suggest that a summer robotics camp encouraged ASD participants to have more social interactions in which robotics was the topic of their conversation.
Type II diabetes (T2DM) is a disease caused by excessive glucose and insulin resistance, and is most commonly observed in obese and inactive adults. Individuals diagnosed with T2DM are often hypertensive; yet, many studies show that physical activity can promote weight loss and a decrease in blood pressure. Furthermore, the temperature, duration and geographical environment in which exercise is performed have been shown to impact the effects of T2DM. We explored a case study that details the duration, time of day and location of physical activity of a 46 year old type II diabetic-male, who has hypertension and is morbidly obese. To test the significance, we used a two sample t-test to compare the systolic and diastolic blood pressures before and after walking; the blood glucose was also compared. Our results show that a significant decrease in systolic blood pressure is observed when the temperature is 70-79 degrees Fahrenheit, as well as walking for 25-34 minutes. There were no substantial changes in the time of day or location in which the walk occurred. In the case of the diastolic blood pressure, the most relevant decrease happens between 60-79 degrees Fahrenheit, 25-29 minutes of physical activity and any time of day in the southern and southeast regions. There was a sustained reduction in blood glucose levels after walking in higher temperatures and after 6 pm. Thus, we conclude that the time of day, location and temperature should be considered to maximize the benefits of physical activity in the presence of T2DM.

While numerous risk factors have been linked to Type II diabetes, few studies have been implemented to look at how risk factors vary across racial/ethnic groups. Thus, we examined how three key psychological stress factors, depression, emotional support and chronic stress burden were associated with Type II diabetes and whether, associations varied across racial/ethnic groups. We analyzed data from adults, 45-84 years from a Multiethnic Study of Atherosclerosis (MESA). We used logistic regression to estimate the association between physiological risk factors and prevalence of diabetes and observing if measures of associations vary by race before and after adjusting income, education and age. Our results indicated there is not a significant correlation between depression and prevalence of Type II diabetes amongst any of the ethnic groups. There is only a correlation between the amount of emotional support one receives and the prevalence of Type II diabetes amongst white individuals. On the other hand, the relationship between chronic burden and the prevalence of diabetes was highly significant across all the ethnic groups. However the strongest point estimate was observed amongst whites. This reveals that the more stressors, not only health stressors but everyday life stressors that any racial or ethnic groups encounter will drastically increase their prevalence to getting diabetes. While our findings did not suggest that these psychological stressors varied by race, they do support and coincide with recent and present work findings that everyday life stressors continue to have an important link to Type II diabetes in the United States.
In 1998, the Institute of Medicine mandated the fortification of folic acid in all wheat and grains in order to increase folic acid consumption in women. Despite this fortification, only 24 percent of women consume the daily recommended amount of folic acid, increasing the chances of developing a neural tube defect affected pregnancy by 50 to 70 percent. In 2004, following a gluten-free diet became an increasing trend for many women across America. Today, the gluten-free market has reached a 6 billion dollar revenue and is steadily increasing. However, studies show that gluten-free diets lack adequate amounts of many micronutrients, especially folic acid. Little to no investigations have been conducted to evaluate if a gluten-free diet meets the daily-recommended amount of folic acid for women. The purpose of the proposed study is to assess the average folic acid content consumed by women of childbearing ages 18-44, who adhere to a gluten-free diet and who attend the University of New Mexico.

Prevalence of vitamin A deficiency (VAD) in broad regions of sub-Saharan Africa and South East Asia remains a significant public health concern. Biofortification is a strategy that has the goal to increase the natural content of pro-vitamin A carotenoids through both conventional breeding and transgenic approaches in staple crops. Ultimate success of this strategy will depend on the stability of pro-vitamin A carotenoids present in these crops and their ability to be incorporated into traditional foods to provide bioavailable pro-vitamin A forms. The objective of this study was to determine the carotenoid profiles of select biofortified maize cultivars at various developmental and storage stages. For pre-harvest stages, carotenoid accumulation prior to harvest at 45 and 52 days after pollination and at harvest day (day 85) were evaluated. For post-harvest stages, effects of storage temperature (4, 25, and 55°C) and relative humidity (13%, 51%, and 76%) on the retention and stability of carotenoids during storage of corn kernels were evaluated. Total Carotenoid Content (TCC) range was 29.25-53.62 ug/g DW. Most cultivars showed (TCC) retention after drying around 102.3-91.74% of pre-drying levels, except for cultivar one cultivar which TCC retention was 52.09%. Accumulation of carotenoids during pre-harvest was highly dependent on variety. For results in post-harvest stages, total carotenoids retention (TCR) after two weeks of storage was highly influenced by temperature, but not by relative humidity (P<0.05). TCR retention in cultivars were 88.65  (4°C), 73.75 (22.5°C) and 54.64 (55°C).
**58 Public Health / Nutrition**  
*Change in Anthropometric Variables with Green Tea Polyphenols*

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This clinical study is a phase II, randomized, double-blinded, placebo-controlled trial in men 30-80 years of age with biopsy proven HGPIN or ASAP and no evidence of prostate cancer, prostatitis or urinary tract infection. The aim of this experiment is to examine the effects of a standardized decaffeinated green tea catechin supplement containing 400mgs of EGCG versus the placebo and seeing if it causes any changes in the body weight and body composition after a 12 month intervention. After a 12 month intervention in men at high risk for prostate cancer, green tea catechin with EGCG, without either inulin or caffeine, showed no changes in anthropometrics. When compared to published studies, green tea catechin without concomitant caffeine or inulin, similar to our study, did not show any benefit in weight reduction or change in any body composition. The published studies were used as comparison points and proved to validate the findings of the research project conducted.

**59 Public Health / Nutrition**  
*Sport Nutrition Knowledge is Insufficient Among Collegiate Athletes*

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**Objective:** The purpose of this research is to analyze an athletes’ sport nutrition knowledge to help better develop sport nutrition education programs.

**Method:** A confidential, anonymous survey questionnaire was completed by student athletes at the Grille at 1810 on The University of Mississippi (UM) campus. The survey consisted of the student’s demographics, who or what they use as a guide for nutrition questions that were scored based on a 100% scale.

**Results:** The overall nutrition knowledge score for college athletes was 39%. Highest among student athletic teams were the volleyball players scored 85% overall. Basketball players scored lowest with 13.33%. When ranked by classification, Sophomores scored highest with overall 60% and freshman lowest with 23.2%. Exercise science majors (47%) scored highest and Pharmacy (6%) and English (5%) majors scored lowest. Confidence level in sport nutrition knowledge, importance of a healthy diet, and quality of eating showed how well the participants believed they knew about sport nutrition and whether or not they had healthy eating lifestyles. Confidence in these three categories was above average with low overall scores this indicates that participants are receiving inaccurate information from sources or the athletes are receiving minimal nutrition education. Athletes do however understand the importance of a healthy diet and quality of eating based on answers given to questions.

**Conclusion:** This study illustrates the current population of athletes at the University of Mississippi is not knowledgeable regarding sport nutrition. This potentially affects their overall performance if accurate nutrition education is not provided and practiced.
Aronia Mitschurinii, also referred to as the black chokeberry, is a fruit-bearing shrub which is native to Maryland. The aronia berry has a dark purple color which can be attributed to the berry’s extremely high content of anthocyanins. Antioxidants are an important nutrient needed for capturing naturally formed free radicals in living organisms, and prevention of oxidation and cancer formation. Aronia’s reputation of being a super berry entices small farms to use it as a perspective specialty crop. The berry’s high content of polyphenols also makes it a likely ingredient in several new products such as, organic teas and vitamin supplements. All these and classic food applications require high temperature pasteurization as a major step during the fruit processing. There are three major effects higher temperatures can have on antioxidants; isomerization, decomposition or the loss of water. Here we present the data for the antioxidant content of Aronia Mitschurinii as a function of the variation in temperature and the time exposed to these temperatures. Detailed measurements and analysis of anthocyanin, flavonoids, polyphenol content and ORAC will be presented and discussed. The aim of this project is to determine the thermal process that would avoid significant decomposition of antioxidants in aronia. This project is supported by the MAES 2013-2014 SEED grant and Thurgood Marshall Undergraduate Research To Retain and graduate Students in STEAM grant.

Lunchables, manufactured by Kraft Foods have constituted a major part of children’s daily lunch consumption since the 1980s. If children did not have the convenient, brightly colored, and enjoyable D-I-Y box in front of them during lunchtime, they were missing out on a popular and exciting way to eat. “Lunchables make lunchtime fun” may be an accurate statement for the nationally renowned product, but are their “fun” food items accurately advertised? The purpose of this experiment was to use the DNA barcode technique to verify the authenticity of common meat types found in Lunchables in the state of Maryland. DNA was extracted from chicken, ham, turkey, and pepperoni found in Lunchables. Using PCR and COI primers, undergraduate researchers amplified about 650bp of the Cytochrome Oxidase 1 mitochondria gene from the samples. The samples were then sent to a company named Genewiz for DNA sequencing. The DNA sequences were analyzed using DNA Subway (The iPlant Collaborative). In conclusion, it was discovered that all meat types originated from the actual meat source (e.g. ham from pig; turkey from turkey). This experiment confirms that Lunchables provide children with a fun and honest choice of meat at lunchtime.
Perovskite solar cells are a promising new class of thin film photovoltaics, with power conversion efficiencies (PCE) of up to 17.9% accomplished in just five years of development. A major aim in realizing the full potential of these devices is the improvement of heterojunction interface dynamics, or the transport of charge carriers from absorber to charge transport layer. It has recently been shown that there is an energy loss in hole extraction at the interface between methylammonium lead tri-iodide (MAPbI3) perovskite and the widely used hole transport material (HTM) spiro-MeOTAD, where an energy offset of 0.4 eV limits attainable open circuit potential (VOC). However, nickel oxide (NiO) has a work function that is well aligned with the MAPbI3 valence band, theoretically allowing for greater VOC (>1.0 V) while providing the additional benefit of being highly stable under illumination. In this study, we tested a room-temperature sputtered NiO HTM in MAPbI3 solar cells, and demonstrate VOC up to 1.03 V, providing a 3% increase compared with literature values for the spiro-MeOTAD system. Additionally, sputter-deposition was compared with solution-processing and shown to produce improved NiO grain morphology and control of conformal film thickness to the nanometer scale. This work represents the first time a NiO HTM system has been employed in a completely planar perovskite solar cell architecture. Preliminary devices demonstrate PCE up to 7%, indicating that while improvements remain to be made, NiO is an intriguing new hole transport material for perovskite solar cells with enhanced photovoltaic performance.

Nanowires form a fascinating topic of inquiry in modern research and offer material properties that are advantageous in fields such as next-generation electronics, solar cells, and optics. When left to self-assemble, nanowires tend to become trapped in metastable assemblies where wire directionality is inhibited by forces such as gravity and solvent interactions. This project explores the introduction of an AC electrical field on particle assembly to order nanowires into nonrandom and reproducible arrangements. Particles were controlled via dielectrophoresis, where induced dipoles oriented wires towards electrode edges and eventually organized them into larger assemblies. The gold electrodes used in experiments were fabricated lithographically using a patterned mask through which the design was projected onto a cover slip coated with positive photoresist. Designs maximized areas of field strength and thus concentrated wires, allowing close-range attraction forces to dictate the assembly process. The nanowires were synthesized through electrodeposition into a porous alumina membrane. This bottom-up method allowed for great versatility in nanowire design, where segments of different materials could be deposited sequentially to create different patterns. A deeper grasp on fundamental nanoparticle behavior could open the possibility of creating ordered assemblies based on rationally-designed wires in the future.
The availability of contaminant-free water is essential to human life and a sustainable society. More than 30% of all human diseases such as cholera, typhoid, etc. result from water-borne contaminants. Although water purification can be accomplished by several different approaches, the resource demands of current approaches limit their widespread use. Distillation is the preferred water purification method; however, the major drawback of conventional distillation is that it is highly energy intensive due to the substantial energy required to boil water. Recently we have demonstrated solar steam generation using nanoparticles dispersed in water. [1]

This approach reduces the dependence on conventional energy sources to essentially zero. In this project we demonstrate solar water purification by distillation using carbon black nanoparticles dispersed in nonpotable water. The solar distillation process successfully kills pathogens and lowers the concentration of dissolved salts of heavy metals to acceptable levels. The solar distillation setup is inexpensive, compact and portable, allowing this technique to be easily deployed in areas where conventional energy resources are limited.


One of the crucial quantities that influences the performance of an organic photovoltaic is the open-circuit voltage. The open-circuit voltage depends on the charge transfer excitation energy between the electron donor and acceptor moieties which form the active material. In this work we present our calculations on the charge transfer excitation energies of tetracene-C60 and rubrene-C60 complexes which were studied experimentally recently. Bilayers of the acenes and the C-60 molecules formed the active material in the experimental devices. Moreover, the charge transfer energies were directly evaluated which provides us an opportunity to directly compare our calculated electronic structure with experiment. In this work we use our in-house methodology called perturbative delta-self-consistent-field method to calculate the charge transfer excitation energy within the density functional theory framework. The tetracene and rubrene molecules have the similar backbone of four fused carbon rings. The rubrene has four phenyl rings which in effect reduces its coupling with the acceptor molecule. We present the electronic structure of the two complexes in face-on and side-on orientations similar to those used in the experimental device setup.
Materials Science
Corrosion Mitigation of Reinforcing Steel in Concrete via Lightweight Aggregate

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Worldwide, corrosion of concrete infrastructure causes over $100 billion in damage each year. Concrete makes up a major portion of infrastructure where nearly five billion tonnes is produced annually — that is approximately one tonne of concrete per person each year. A major concern, however, is the premature deterioration of the concrete. Corrosion is initiated by exposure to aggressive media (e.g. chloride ions from deicing salts or seawater) which depassivates the steel. Expansive products such as iron oxide are then created, eventually cracking and spalling the concrete cover and reducing the service life of the structure. Cinnamaldehyde, a bioactive agent derived from cinnamon bark, can mitigate the corrosion of metals but has a negative effect when included in a cementitious matrix. Pre-soaking bioactive agents in lightweight aggregate (LWA - commonly used in ‘internal curing’ and lightweight concretes) can prevent this interference. Experimental results show that the addition of the cinnamaldehyde-soaked LWA performs 91% better under accelerated corrosion test conditions. These findings indicate the service life of structures may be prolonged in corrosive environments.

Poster Presentations
**Poster Presentations**

**Physics and Astronomy**

**2D Self Assembly of Colloidal Membranes using Three Component Virus and Polymer Mixtures**

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The entropy driven self assembly of colloidal membranes is displayed by attractive interactions of virus-like rods in the presence of depletants. We have explored these interactions by mixing polymers at higher and lower molecular weights with viruses that have different lengths. We mixed the hypothesized polydisperse polymer with the monodisperse polymers at higher and lower molecular weights to see if molecular weight or monodispersity mattered more in membrane formation. It was concluded that membrane formation does depend on the molecular weight distribution because the greater the molecular weight, the greater the range of attraction amongst rods. We also mixed rods at different lengths to see phase separation in the samples. With the usage of fluorescent dye, we were able to see regions of the sample that were rich with each virus. This research opens up a door for further exploration of virus mixtures at different lengths and polymer mixtures at varying molecular weights in colloidal membrane formation.

**Cancer Biology**

**Medicinal Mushroom Reishi and Lapatinib Decrease the Viability in HER2+ Inflammatory Breast Cancer Cells Line**

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Inflammatory Breast Cancer is the most lethal and rare form of breast cancer. This cancer accounts for five percent of the cancer cases in the US and PR. IBC is most commonly either triple negative, ER-, PR- and HER2- or ER-, PR- and HER2+. There is no specific IBC treatment; thus, it seems feasible to find a therapeutic for this deadly disease. Our published data demonstrates that Ganoderma lucidum (Reishi) inhibits the viability of the triple negative IBC SUM149 cell line, but not of MCF10A noncancerous mammary epithelial cells. We aimed to investigate Reishi effects in the viability of the ER-, PR-, HER2+ IBC cell lines. Also we will investigate the effect of Reishi and the HER2 Tyrosine Kinase Inhibitor, lapatinib on IBC cells. Our hypothesis is that Reishi inhibits cancer cell viability and sensitizes IBC cells to lapatinib therapy. Herein, SUM190, KPL-4 and IBC3 cells were treated with increasing concentrations of lapatinib and/or Reishi for 24 or 72h. The combination of lapatinib plus Reishi reduced cell viability of SUM190 cells to 70% when treated with a concentration of 0.5mg/mL Reishi for 72h. Also, our data shows a reduction in cell viability of 80% in KPL-4 cells treated with lapatinib plus Reishi for 72h. We are currently directing our efforts to continue studying the contribution of Reishi in IBC cells and to continue studying the molecular and signaling the contribution of Reishi in IBC cells when treated with lapatinib after 24 or 72h.
**MicroRNA-Mediated Regulation of Human Serine Palmitoyltransferase-1 Gene Expression in Cancer Cells Responding to Stress**

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The discovery of microRNAs, miRNAs, has helped identify a new class of non-protein-coding, endogenous, small RNAs that play important roles in regulating gene expression. Recent studies indicate that the human serine palmitoyltransferase-1, SPTLC1, protein is stress responsive and cells expressing a C-terminal modified variant of the gene acquire altered stress response behavior that promote survival and progression of the malignant phenotype. However, the molecular mechanism regulating gene expression required for the encoded SPTLC1 protein variant that plays a role in cancer survival and progression has not been investigated. To link microRNA regulation with gene expression, the current study examines the expression of SPTLC1 alternate open reading frame in cells exposed to 42°C heat shock. The inflammation-associated human prostate cancer, PC3 and brain tumor, Glioma LN18, cell lines, were treated in the presence of inhibitor or mimic of the miR-137 microRNA, which is known to target the SPTLC1 gene. It is hypothesized that miR-137 plays a role in regulating the differential expression of SPTLC1 during cellular response to heat shock stress. The expression of SPTLC1 was assessed in untreated and treated cells by quantitative reverse transcription PCR. The expression of SPTLC1 alternative ORF in untreated cells is about two-fold higher in SPTLC1 recombinants compared to the parental cell line. Data generated from this study will help provide new insight into functional genomics aspect of SPTLC1 that may be helpful in better understanding its role in the progression of inflammation-associated cancer cells.

**Histone Deacetylase Inhibitor Treatment Increases Thioredoxin Interacting Protein in HCC Cells**

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Hepatocellular carcinoma (HCC) is the third most common cause of cancer related deaths in the world. Thioredoxin interacting protein (TXNIP) is a tumor suppressor that has pro-apoptotic, anti-proliferative properties. The expression of TXNIP is reduced in HCC, but the mechanism by which this occurs is unknown. Epigenetic regulation of gene expression, such as histone modification, is common in HCC. Trichostatin A (TSA) inhibits histone deacetylase proteins in chromatin. This results in chromatin uncoiling, allowing transcription factors to access DNA and regulate gene expression. This study’s focus is to determine whether TXNIP expression is regulated by histone modifications in an HCC cell line. It was hypothesized that that TSA treatment will increase TXNIP expression. We tested our hypothesis in vitro. Huh7 cells, a HCC cell line, were cultured and treated with TSA at 0.5μM, 1μM, and 2μM concentrations for 24h. TXNIP mRNA and protein were extracted and quantified by Nanodrop 3000 and Bradford assay respectively. cDNA synthesis was performed using the Superscript III kit (Invitrogen). Quantitative RT-PCR for TXNIP and GAPDH was performed using the ABI-Taqman system. Western Blot and Image J software were used to measure TXNIP and beta actin protein expression. Student’s t-test was used to test for significant differences. TSA treatments resulted in a significant increase in TXNIP mRNA expression. Immunoblots indicate increased TXNIP protein in the TSA treated cells. Supportive of the hypothesis, TXNIP expression in HCC may be regulated by epigenetic mechanisms and treatment with TSA increases TXNIP expression.
Cancer Biology

Preclinical Studies Using Bioactive Compounds to Develop Novel Chemoprevention Strategies for Breast Cancer

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Breast cancer is the most common type of cancer among women in the United States. Despite the impressive progression of therapies and advanced treatments, there is still a great need for novel therapeutic discoveries. Cellular studies have provided insights into the benefits of using bioactive compounds to combat breast cancer. One bioactive compound that is of interest is cruciferous vegetable constituent benzyl isothiocyanate (BITC), which our lab has previously shown to present substantial protection against mammary carcinogenesis in a transgenic mouse model through its inhibition of the effects of adipocytokine leptin. Leptin is overexpressed in obese breast cancer patients and is known to increase tumorigenesis via multiple signaling pathways. BITC treatment circumvented the leptin-stimulated growth and migration. The present study provides evidence that BITC not only inhibits oncogenic adipocyte-derived hormone, leptin, but it also upregulates a protective hormone, adiponectin, and inhibits stemness markers (e.g., KLF4 and SOX2) to minimize the oncogenic progression of the cells. Increased adiponectin impairs adipocyte differentiation, which impairs leptin's function in cell proliferation. The results of this study serve to show that BITC treatment in the human breast cancer cell lines MDA-MB-231 and MCF-7 elevate the expression of adiponectin and decreases the expressions of stemness biomarkers SOX2, NANOG, KLF4, and OCT4. The methods used to show these results include treating the cultured cell lines with BITC, using western blot analysis, PCR analysis, and mammosphere assays. Taken together, these results may provide evidence that BITC could develop into a novel chemoprevention strategy for breast cancer.

Cancer Biology

Biological Evaluation of Novel Pyridine-Bridged Analogs of Combretastatin-A4 as Anti-cancer Agents

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Inhibition of tubulin polymerization disrupts the formation of tumor vasculature, making the microtubule cytoskeleton an effective target for cancer chemotherapy. In this project, a prototype agent called Combretastatin-A4 (CA-4) was used to design analogs to disrupt the vasculature. The compound attaches to the colchicine binding site of tubulin to block assembly, and causes rapid vascular shutdown that leads to cell death of tumor cancerous cells. Dr. Guangdi Wang and colleagues in the Chemistry Department of Xavier University developed, designed, and synthesized over 30 novel pyridine-bridged analogs of CA-4. We hypothesized that some of the compound analogs would inhibit cancer cell growth, induce cell cycle arrest, and block angiogenesis. Our group tested the compounds for their effectiveness as a possible cancer therapeutic agent similar to CA-4. We tested the compound in vitro for tubulin polymerization, antiproliferation, cell cycle progression, and ex ovo for inhibitory effect on angiogenesis. We found two analogs 4h and 4s successfully inhibited tumor cell survival, arrested cell cycle progression, and blocked angiogenesis. Thus, these analogs may be potential cancer therapeutics for advanced stage cancer.
Prostate cancer is the leading form of non-skin cancer in American men and the second leading cause of deaths behind lung cancer, with African American men having the highest incidences and mortality rates. Genistein, EGCG, and lycopene are phytochemicals that demonstrate chemotherapeutic properties in prostate cancer cells. Therefore, we hypothesized that genistein, EGCG, and lycopene will decrease the growth of LNCaP prostate cancer cells through apoptotic induction and that combining these phytochemicals will have an additive effect on this process. The LNCaP prostate cancer cells were treated with the phytochemicals in single and combination treatments for 24 and 48 hrs. MTT assay was used to measure the viability of the cells post treatment, while apoptosis and caspase assays were used to determine the mechanism of action of phytochemical-induced cell death. Our results indicated that EGCG was more effective at all concentrations and that all the phytochemicals were effective inducers of apoptosis in LNCaP prostate cancer cells. Combination treatments showed an additive effect, and cell growth decreased as time progressed for both the single and combination treatments.

Gene-altering compounds are considered potential therapeutic tools in the treatment of various cancer tumors. Histone deacetylase inhibitors such as sodium butyrate (NaBu) and the DNA methyltransferase inhibitor 5-azacytidine (5-azaC) regulate cell survival and differentiation of cancer cells by yet to be fully understood mechanisms. Changes in intracellular calcium could potentially regulate cell survival and differentiation by gene-altering compounds. It is becoming evident that T-type calcium channels constitute an important route for calcium influx in tumor cells that can trigger changes in cell proliferation and differentiation. This work was designed to test whether NaBu and 5-azaC promotes the expression of T-type Ca2+ channels in prostate cancer cells. Our study demonstrates that NaBu increases the expression of the Cav3.2 T-type Ca2+ channel subunit by a transcriptional mechanism. The effect of NaBu on Cav3.2 protein expression was concentration-dependent. NaBu stimulates the expression of the Cav3.2 T-type Ca2+ channels both in an androgen-dependent (LNCaP) and an androgen-independent (PC3) cell line. Inhibition of T-type Ca2+ channels had no effect on the number of apoptotic cell number. Further experiments will seek to determine the effect of 5-azaC on T-type Ca2+ channel expression. These results demonstrate that gene-altering compounds can regulate the expression of T-type Ca2+ channels.
Progression of prostate cancer is dependent on the androgen receptor (AR). The cochaperone FKBP52 is an important factor which plays a critical role in maintaining AR in a functionally folded state, thereby facilitating receptor hormone binding, receptor translocation to the nucleus, and receptor-mediated gene expression. All current anti-androgen therapies block hormone binding to the receptor thereby terminating transcription of AR-responsive genes and, thus halting tumor progression. In late stage castration resistant prostate cancer (CRPC), hormone may no longer be essential rendering current therapies ineffective. Therefore treatments that do not strictly target hormone binding are critically needed for the treatment of CRPC. By targeting the interaction between FKBP52 and AR, activity can be suppressed irrespective of hormone binding. In this study in silico modeling was used to select compounds that theoretically should interact with and disrupt FKBP52 regulation of AR activity. Promising candidate compounds were tested both alone and in combination with currently approved therapies for activity using a luciferase reporter assay. Drug combinations hold the potential to act synergistically in decreasing AR-mediated activity compared to single drug therapy. Mda-kb2 cells, which contain an AR- and GR-responsive luciferase reporter gene were used to generate dose response curves to determine single drug and drug combination efficacy. To date preliminary data has not exhibited any synergism with the tested drug combination. Ultimately these studies will support the testing of selective AR inhibitors both as single drug treatments and as a combination therapy for the treatment of CRPC.

Plants are stationary organisms that must constantly respond to a changing environment in order to survive. Primary detection and response to drought and flooding occurs in the roots. However, how the specific cell types of the roots respond to these stresses is not completely understood. Our lab utilizes two techniques, INTACT (Isolation of Nuclei TAgged in specific Cell Types) to isolate DNA and RNA present in nuclei, and TRAP (Tagged Ribosome Affinity Purification) to isolate translating ribosome from the cytoplasm, in order to study, in detail, how plants responds to environmental cues. For this work, we used Arabidopsis thaliana promoters to drive expression of NTF (Nuclear Targeting Factor) or TRAP in specific cell types of Medicago truncatula, alfalfa, roots in order to study how alfalfa responds to flood stress. Our results show that all of the A. thaliana promoters, with the exception of AtWOX5, had the same time and place expression in M. truncatula as in A. thaliana. We also show that INTACT and TRAP can be performed using M. truncatula tissues, which has not been shown before. We are currently characterizing the gene response of alfalfa root cells to 2 hours of flooding stress. The transcriptional and translational response to flood stress in alfalfa will be compared to tomato and rice. The long-term goal of this research is to establish a comprehensive understanding of how crops respond to a variety of growth conditions so that this information can be used to develop hardier crops.
Thymic Epithelial Cell Aging is Determined by the p63-FoxN1 Regulatory Axis

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The postnatal thymic epithelial progenitor (TEP) pool is proposed to be regulated by the p63 and FoxN1 genes through proliferation and differentiation, respectively. However, the combined role of these two genes in the aging TEP is still a mystery due to the complexities of overlapping pathways. Evidence from murine models has elucidated contrasting roles of the p63 isoforms during the aging process. We found that TAp63+, but not DeltaNp63+, thymic epithelial cells (TECs) were increased with age, accompanied with increased senescence associated beta-gal clusters, p21+, and p16+ TECs. Senescent clusters also developed after intrathymic infusion of exogenous TAp63 cDNA into young wild-type mice. Using our conditional FoxN1 gene knockout mouse model to disrupt TEP differentiation accelerated this senescent phenotype to early middle age. However, upon infusion of exogenous FoxN1 cDNA into aged wild-type mice resulted in only an increase in DeltaNp63+ TECs, but no change in TAp63+ TECs in the partially rejuvenated aged thymus. Interestingly, using a novel FoxN1 gene transgenic mouse model to enhance TEP differentiation, DeltaNp63+ TECs were decreased in young thymus. Additionally, the TAp63+ population contained a high percentage of phosphorylated-p53 and apoptotic TECs, but showed no changes in BrdU-labeled proliferation. As a result, FoxN1 controlled TEC differentiation as a bottleneck to determine TEP pool via affecting TAp63 and DeltaNp63 levels. Thus, TEC homeostasis during aging has been determined through the p63-FoxN1 regulatory axis.

Determining the Roles of Histone Variants HTAS-1 and HTZ-1 During Spermatogenesis in C. elegans

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Male infertility affects 40% of infertile couples in America. Disruption of chromatin integrity is a major cause of infertility, hence histones play an important role in maintaining this integrity as they package DNA into nucleosomes composed of the canonical histones H2A, H2B, H3, and H4. Though the purpose of histone variants is unclear, they are highly conserved across many species, indicating they have evolved to sustain important functions in different tissues. For example, in C. elegans, histone variants such as HTZ-1 and HTAS-1 replace canonical histones throughout meiosis. The evolutionarily conserved HTZ-1 is ubiquitously expressed, while HTAS-1 is sperm-specific. htz-1 mutants are sterile and htas-1 mutants have a decrease in progeny, each suggesting a role in spermatogenesis. Though very similar to H2A, these histone variants differ greatly in their N-terminus and C-terminus domains, sites where histone modification typically occurs, as well as in their core domain, known to associate with DNA. We hypothesize that these domains are the basis of each variant’s function in different developmental processes, including spermatogenesis. To address this, different chimeric histones will be created to express varying combinations of these domains, joined into the rest of the canonical H2A protein. Through in vivo analyses, we can test which domains are necessary for an increase in progeny in mutants lacking the respective histone variant. These results will elicit which differences in their amino acid sequences uniquely corresponds to their function in different cell types, and help define broad features of histone variants important to their function across species.
**Poster Presentations**

**Developmental Biology**

**Bringing Up the Rear: Septins, Fatz, and Collective Cell Migration**

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The Drosophila melanogaster egg chamber is an ideal model system that can be used to study tissue elongation. Egg chambers are mostly spherical in early stages, but they begin to elongate during mid-stages, and are elliptical in late stages. Collective follicle cell migration is required for egg chamber elongation. Before the follicle cells migrate, actin is planar polarized at the basal surface, perpendicular to the elongating (anterior-posterior) axis. This polarization allows for directional, collective migration of the follicle cells along the ECM. In the absence of migration the egg chamber will not elongate. Recent research suggests that the septin family of proteins, most well-known for their function in cytokinesis, may function as the fourth class of cytoskeletal filaments that may play a role in cell migration and tissue elongation. The primary investigation is if septin localization is disrupted in fatz mutant follicle cells, as Fatz is an infrequently studies atypical cadherin that is one of the most well known regulators of follicle cell migration. During the fatz mutant cloning process, we unexpectedly found that actin protrusions are lost in fatz null mutant clones. This lost of actin protrusions may suggest that Fatz, with its large extracellular domain, may regulate forward movement of the cell behind. Further investigation is currently underway to better understand this relationship. If researchers can better understand the role of Fatz and actin in follicle cell migration they can apply this knowledge to the future study of tissue elongation and tissue engineering.

**Environmental Health Sciences**

**Bumble Bees of Kanawha County, WV, with Emphasis on Two Endangered Species**

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Bumble bees (genus Bombus) are wild pollinators that are important, from an ecological and economic standpoint. They pollinate many species of plants; these plants depend heavily on bumble bees to pollinate them. Many Bombus species are suffering from severe population declines. Research on Bombus populations will help us understand the cause of their sudden decline. The goal of this project is to assess the diversity of Bombus in two counties in West Virginia: Kanawha and Mercer. Of particular interest to our research was the critically endangered Bombus affinis and Bombus terricola. The results of this study will provide insights to the local diversity and abundance of these insects, potentially reveal refugia, and contribute to our understanding of their decline. For this study, we captured and identified foragers from many different sites and a various habitats. We collected data on the following: species identities, frequency, the location and type of habitat. These data enabled us to explore the demographics and distributions of these species in our study areas. Our data were compared to museum specimens in order to determine population shifts during the period of decline. Our data showed trends of decline of the subgenera Thoracobombus and Bombus (s.s), and robust populations of species in the subgenera Pyrobombus and Cullumanobombus. An interesting find was a high abundance of Bombus auricomis in Kanawha County, a species that has been declining in other areas. This finding suggests that the southern part of West Virginia may be a refuge.
Environmental Health Sciences

Cr(VI) Resistance of Wastewater Bacterial Isolates

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Bioremediation is the treatment of pollutants and waste by the use of microorganisms that break down the undesirable substances. Chromium is used in industries such as metallurgical (alloy, and steel), chemical (pigments and tanning) and refractory (chrome and chrome magnesite) industries. Chromium has two main oxidation states, Cr (III) and more carcinogenic Cr (VI). Cr (VI) is mainly used for its anti-corrosive properties. Influent is the raw material that enters the plant through the collection system. Sludge is the growth of microorganism to break down suspended solids. The purpose of this research is to isolate and characterize bacterial isolates from wastewater environmental samples and determine if the bacterial isolates are resistant to Cr (VI). Influent and sludge samples were collected from a local wastewater treatment facility, serially diluted and plated onto brain heart infusion agar. After two days of incubation, the unique bacterial colonies were re-streaked. Of the eight sludge isolates, S14 were resistant to at least 200 ppm of Cr (VI) using a plate assay. Of the six influent isolates I4 were resistant to at least 100 ppm of Cr (VI). Growth of three sludge isolates (S3, S11, and S14) in liquid culture reveal that S3, S11, and S14 grew in 50 ppm, 25 ppm, and 200 ppm of Cr (VI), respectively. Future experiments are to test the isolates for Cr (VI) reduction.

Environmental Health Sciences

Motivational Messages for Increasing Cancer Prevention in the Community: A Pilot Evaluation

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Reports show that cancer is the second leading cause of death in the United States. Cancers related to tobacco use, excessive alcohol use, and an unhealthy diet and no exercise can be prevented with a healthy lifestyle. The aim of this study is to design cancer prevention messages and evaluate their effectiveness in motivating healthy behaviors in customers of the Northeast Market in Baltimore MD. Fifty participants viewed a brief show on cancer prevention behaviors and were asked to complete a survey evaluating the presentation. It was hypothesized that the messages would positively encourage healthy behaviors in the customers. One hundred percent of participants answered that the prevention messages were informative and ninety-six percent of participants answered that the messages were successful in motivating a behavioral change. Participants also made suggestions to the presentation, which included: adding sound, and providing information on salt intake and serving sizes of common foods. It is hoped that the study findings will improve future presentations, reach individuals on a larger scale, and ultimately decrease the number of preventative deaths by cancer among Baltimore residents.
Heavy metal contamination continues to cause serious environmental impacts including damage to human health. Sources of heavy metal contamination are widespread, especially in urban environments. Certain plants such as sunflowers have been shown to sequester lead in their root systems, helping to filter lead out of soils, a process called rhizofiltration. In this project, we added B. megaterium to the root system of sunflowers growing in lead contaminated soil and examined the efficiency of rhizofiltration. Lead levels in the rhizosphere of the amended plants were almost 100 ppm higher than those without the treatment, suggesting the amendment may have been effective in augmenting lead sequestration. In addition to evaluating lead levels, we conducted preliminary phylogenetic assays of the soil with and without the presence of the plant. Although complete coverage of the community phylogeny was not possible, the changes that the rhizosphere may have prompted in community composition were evident. These studies may suggest simple methods for enhanced bioremediation in a growing sector of agriculture.

Introduction: Indoor swine rearing facilities harbor high levels of dust containing various microparticles and microorganisms (e.g., bacteria, fungi, dander, feces), endotoxins and ammonia. Over time, repeated exposure to these particles initiate chronic respiratory issues increasing the predisposition to develop respiratory complications like COPD and asthma. Interestingly, pigs within these facilities do not display an apparent aversion to the dusts, unlike farm workers. Oxidative stress is a key feature of chronic respiratory diseases. We hypothesize that swine barn dust exposure facilitates oxidative stress in pneumocytes.

Methods: We employed human alveolar adenocarcinoma A549 cells to test our hypothesis. A549 cells were in media only or exposed to 1%, 3% and 5% swine dust extract (DE) for 1, 8 and 24 hours. Endpoint assays to detect oxidative stress and toxicity included Live/Dead viability, Amplex Red for hydrogen peroxide/peroxidase generation, lactate dehydrogenase activity and Griess assay for nitric oxide production. Results: After 24 hours of exposure to swine barn DE increased production of reactive oxygen/nitrogen species compared to 1 and 8 hours. There was a trend of dose-dependent differences in reactive oxygen/nitrogen species production; however, these levels did not reach formal significance. These findings were consistent with observations of cultures of A549 cells exposed to lipopolysaccharide, a component of swine barn dust and DE.

Conclusion: Taken together, these results and observations indicate that exposure to swine barn dust may activate oxidative stress pathways in the lungs. These preliminary studies provide insight into mechanisms governing development of agriculture related respiratory diseases in farm workers.
Au can be used in treatment of cancer in nano form to target cancerous tissues. Anti-cancer biodrugs can be coated onto the Au. However, two problems exist. Firstly, nanoparticles aggregate in vivo and are cleared by the immune system. To prevent this, the nanoparticles must be separated. Secondly, biodrugs are made from the same biomolecules that make up the body, as such; they are subject to enzymes that degrade biomolecules in the body. This leads to indiscriminate distribution, degradation, and a risk of under-medicating. To compensate, a larger dose of the biodrug is given; however, toxicity becomes the risk. Certain peptides (nano-tags) bind Au. We hypothesize that displaying these nano-tags on the surface of our bacteriophage Q-Beta, will allow them to bind Au, preventing aggregation. This Au can then be coated with an anti-cancer biodrug, and the Au will convey protection to the biodrug. To achieve this, the genes of three gold-binding peptides: Au0 (LKAHLPPSRLPS), Au1 (VSGSSPDS), and Au2 (TGTSVLIATPYV) were inserted separately into the genome of Q Beta at the end of the A1 gene. The resulting recombinant phages, pQBetaAu0, pQBetaAu1 and pQBetaAu2, were transformed with HB 101 E. coli. Plaque assay provided the titer and phage morphology, and RT-PCR confirmed the tag gene size for each construct. Binding assay allowed different concentrations of Au to bind to the recombinant phage. Confirmation and visualization of the phage-nanoparticle complex was verified via Transmission Electron Microscopy (TEM). The next phase is to focus on coating the Au nanoparticles with chemotherapeutic biodrugs.

The human immunodeficiency virus (HIV) has been a prevalent problem around the world for many years. Since HIV is a retrovirus, it has a high mutation rate. Due to its capability to mutate, creating a form of defense against the virus has posed major problems. Currently, Highly Active Antiretroviral Therapy (HAART) is being used to lower the viral load in infected patients, but there are still patients in developing countries that continue to show symptoms while on this combination of medications. From this we conclude that the increase in viral load in patients taking the antiretroviral drugs indicates drug resistance. At different times during treatment, the cDNA from infected patients in Peru was purified from their blood samples and quantified using qPCR. The results show an increase in viral load in those patients. We propose that a new effective way to detect the change in viral load of those patients would be through the use of the RNA phage display system. The membrane proximal external region (MPER) of the HIV virus represents a major antigenic region of the virus. MPER gene was constructed and successfully displayed on the RNA phage surface. The hybrid phages Q-BetaMPER were used to evaluate antibody titer from the same patients through a quantitative ELISA. Preliminary data shows increasing titer of antibodies. Although these results still need to be confirmed, it is the first study to our knowledge on HIV infection. This novel technology can be extended to vaccine development and other viral pathogenesis studies.
### Poster Presentations

#### Neuroscience

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<th><strong>Kappa-opioid Receptor Antagonist Anxiolytic Effect on Stress and Exercise</strong></th>
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Department of Psychological Sciences, University of Vermont, Burlington, VT; Division of Social and Behavioral Sciences, Nova Southeastern University, Davie, FL

There are many beneficial qualities to exercise, including reducing anxiogenic and depressive symptoms caused by stress in humans and rodents. Studies show that stress prior to exercise interferes with the anxiolytic effect of exercise. Accumulating evidence indicates kappa-opioid receptors (KORs) and their endogenous opioid, dynorphin, modulate the stress response. NorBNI, a KOR antagonist, has anxiolytic and antidepressant qualities, suggesting it can be utilized to block the negative effects of stress to salvage the effects of exercise. The goal of this study is to assess whether norBNI administered prior to stress will prevent stress from interfering with the anxiolytic effects of exercise. The acquisition of neither exercise nor the distance ran was affected by norBNI over a fourteen day period. Exercising groups showed blunted and reduced immobility times on days one and two of a test measuring depression while norBNI groups showed a reduction in a fourteen day protocol to measure anxiety. These findings propose norBNI does not interfere with exercise, the antidepressant effects of exercise and may have a short term or additive anxiolytic effect.

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<th><strong>Early Behavioral Voiding Patterns Predict Long-term Urinary Dysfunction After Spinal Cord Injury</strong></th>
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Spinal cord injury (SCI) can result in devastating neurologic deficits. Among these, impaired lower urinary tract function (LUT) ranks as a leading cause of morbidity. Clinically, LUT impairment demonstrates variable dysfunction with some showing partial recovery of spontaneous bladder emptying via incomplete pathways. Little experimental research, however, has investigated mechanisms that correlate with long-term dysfunction versus recovery. Development of translational therapies for improving LUT function after SCI depends on identifying early predictors of chronic disease. Therefore, the purpose of this study is to examine longitudinal LUT function after experimental SCI to determine predictors of longterm dysfunction.10 rodents underwent mid-cervical contusion. Voiding behavior was assessed pre-injury and 4, 6, 8, 12 weeks post-SCI using chromatographic evaluation of normal vs. abnormal bladder emptying. Bladder cystometry and sphincter EMG were performed at 12 weeks post-SCI to assess for dyssynergy and supraspinal-spinal neuronal connectivity. Bladder wall histology and elastin content were evaluated for functional changes related to chronic urinary retention. All animals demonstrated acute LUT dysfunction after cervical contusion. Non-volitional behavioral voiding at 4 weeks post-SCI correlated with persistent abnormal bladder contractions and sphincter EMG dyssynergy at 12 weeks, and with increased bladder muscle hypertrophy and elevated elastin. Conversely, spontaneous recovery of volitional behavioral voiding at 4 weeks correlated with normal bladder contractions and sphincter EMG synergy at 12 weeks, and more normal bladder muscle histology and elastin content. Therefore, early behavioral voiding by 4 weeks post-SCI predicts likelihood of recovery. Development of therapies may consider evaluation of these early predictors in future studies.
Serotonin (5-HT) is a modulatory neurotransmitter in the central nervous system that plays a role in many physiological responses by binding to 14 receptor subtypes. The 5-HT2C receptor (5-HT2CR) subtype, a 7-transmembrane spanning G protein-coupled receptor, is involved in neuronal excitability, spatial learning, mood, and appetite. This receptor activates signaling pathways downstream of the Gaq/11 protein and other intracellular proteins that activate G protein-independent pathways. The structurally similar 5-HT2A receptor can additionally activate the G protein-independent JAK/STAT pathway. The purpose of the present study was to investigate the ability of the 5-HT2CR to activate the JAK/STAT pathway as well.

Human Embryonic Kidney (HEK) 293 cells were transfected with human 5-HT2C receptor and stable cell lines were generated. Cells were treated with serotonin or vehicle. Proteins were separated by SDS-PAGE gel electrophoresis and levels of phosphorylated JAK2 and STAT3 were analyzed via western blotting. Constitutive activation of JAK/STAT signaling was observed in cells containing the 5-HT2CR, while activation was not observed in untransfected cells. Treatment with 5-HT increased levels of phosphorylated JAK2 and STAT3, indicating that agonist binding enhances JAK/STAT activation. This is the first report of the 5-HT2CR activating this pathway and suggests that this receptor may be involved in growth, cell differentiation, the immune response and transcription of other STAT activated genes. Future studies will examine activation of this pathway in the presence of other 5-HT2CR agonists and antagonists, and whether naturally occurring single nucleotide polymorphisms in the human 5-HT2CR alter signaling.

— Supported by NSF Grant HRD-1238723 to HMF
**Poster Presentations**

**Neuroscience 111**  
**fMRI Study of Working Memory Networks in Prodromal Schizophrenia in Response to nAChRs Blockade**

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Geoffrey Schaubhut,  
Sarahjane Dube,

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Department of Kinesiology, California State Polytechnic University, San Luis Obispo, San Luis Obispo, CA;  
Department of Psychiatry, University of Vermont, Burlington, VT

Individuals with schizophrenia (SZ) have a pronounced cognitive deficit in working memory (WM), which is present to a lesser degree in individuals with prodromal schizophrenia (PRO), which is an early stage of SZ. Studies indicate alterations to the nicotinic acetylcholine receptors (nAChRs) could account for the altered functional neural circuitry and poor cognitive task performance seen in SZ. SZ onset could be characterized by describing the effects of PRO and a nAChRs blockade on WM using functional MRI (fMRI). 11 non-smoking PRO and 11 control subjects (CTRL) between 18 and 26 years old performed the N-back task, which assesses WM (0-back, 1-back, 2-back, and 3-back conditions) during an fMRI scan. On two separate days participants were randomly administered 20-mg of mecamylamine (MEC) or placebo (PLC) before undergoing an fMRI scan. In response to MEC, but not PLC, PRO are statistically significantly slower in hit-reaction time (HRT) across all N-back conditions compared to CTRL. This study found in response to PLC, PRO and CTRL fMRI results indicated similar activation of areas associated with the WM network. A group difference using the 2-back minus 0-back contrast was observed in the left inferior frontal gyrus (IFG), which coincides with the performance reflected in the HRT in response to MEC. PRO did not recruit the IFG when performing the N-back task, unlike CTRL, who recruited the IFG and left middle temporal gyrus. This indicates non-smoking PRO nAChRs could be more sensitive to MEC, perhaps demonstrating altered nAChRs function in PRO.

**Neuroscience 112**  
**Effects of Social Stress on Fetal Development and Growth in Female Rhesus Macaques**

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Amanda Mummert,  
Jodi Godfrey,

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A large body of epidemiological data demonstrates a connection between early life health status, including size at birth and growth trajectory, with risk of chronic disease later in life. One potential mechanism underlying these effects on fetal development is exposure to chronic psychosocial stress (CPS), which in adults has been associated with poor health outcomes. Less is known, however, about how maternal exposure to stress during pregnancy impacts fetal development and infant birth outcomes. To investigate how maternal CPS during pregnancy affects fetal growth and infant body size, we employed a socially housed rhesus macaque model of CPS (n=13). Previous research has demonstrated that subordinate females are less likely to become pregnant, and their pregnancies have negative outcomes. We hypothesize that dominant maternal rank will correlate with larger offspring size when compared to subordinate maternal rank, evident during gestation in femur length and at birth in terms of weight, length, and abdominal circumference. To evaluate maternal size, adult females were examined at Day 100 of gestation and immediately after birth. For results evaluation we statistically compared the measurements from dominant and subordinate subjects in order to evaluate significant differences between these groups. Our results showed that maternal rank had no statistically significant effects on the anthropometric measures of the infant. We believe that our hypothesis was not supported due to the small sample size available at this time point. However, our analysis revealed unexpected and interesting results that can inform future studies and contribute to general scientific knowledge.
The Effect of Pre-training on Hippocampal Cognition in a Rat Model of Malformation of Cortical Development

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Pediatric patients with indications of cognitive impairments often display malformation of cortical development (MCD) that can lead to epilepsy. In our lab, we investigate learning and memory disorders that may or may not be caused by epilepsy, with a general focus on the pediatric period, and on whether training can improve cognition. For decades, many believed that epilepsy had a direct correlation to learning impairments but never knew the etiology behind this reasoning. We investigate the connection between epilepsy and cognitive deficits by performing cognitive tests on adult Sprague-Dawley rats that have cortical malformations. This is done by injecting a pregnant dam with Methylazoxymethanol acetate (MAM) leading to malformation in the hippocampal region of the brain in the pups. Water maze test are performed using MAM and control rats to view and compare their behavior in the realms of learning and memory. Our results suggest that pre-training did not improve spatial deficits. We divided control and MAM exposed Sprague-Dawley rats into enriched and non-enriched groups. The pre-trained group underwent prior delayed non-match to sample (DMNS) testing. The goal of our study is to know if pre-training can enhance the performance of rats in a memory test. By doing so, we can target the areas where cortical malformations might have occurred in the brain and improve hippocampal cognition through cognitive pre-training in other task. Ultimately, with this data, this can lead us to be able to evaluate the substrate of the seizures or the etiology that causes these seizures in pediatrics.

Diphenyl Ditelluride Induced Neurotoxicity

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Tellurium compounds have been used in the vulcanization of rubber, in metal oxidizing solutions used to blacken or tarnish metals, and in the nanoparticulate semiconductor industry. Moreover, the use of these compounds will increase due to their importance as catalysts in inorganic and organic synthesis, as stabilizers for polymers, as components of insecticides and phase-change optical magnetic disks, and as compounds used in the photography industry. The risk for occupational as well as environmental exposure to these compounds may be implied due to increased usage of these compounds. One tellurium containing compound, diphenyl ditelluride (DPDT) has been demonstrated to cause behavioral impairments, inhibit glutathione peroxidase (GPx), and increase lipid peroxidation (a marker of oxidative stress) in whole brains taken from mice. The neurotoxic effects of DPDT on specific brain regions have not been explored. In the present study, we will determine if brain regions have different vulnerabilities to DPDT induced neurotoxicity. Using C57BL6 mouse pups at age Po-P1, we will prepare primary neuron-glia co-cultures from various brain regions. We will assess the neurotoxic effects of DPDT in the various co-cultures by assessing cytotoxicity, mitochondrial toxicity, reactive oxygen species production, and GPx activity. The findings from these studies will provide insight into the vulnerabilities of various brain regions to DPDT induced neurotoxicity, and possibly raise the awareness of the potential neurotoxic outcomes after exposure to DPDT.
Pharmacology
Role of Anoctamin-1 in Endothelial Cell Apoptosis

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Ayed Allawzi,
Gaurav Choudhary

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Department of Chemistry/Biochemistry, Hunter College, CUNY, New York, NY

Pulmonary Arterial Hypertension (PAH) is a disease characterized by the elevation of pulmonary vascular pressure that can lead to heart failure if untreated. Abnormal cell proliferation is a key step in the progression of the disease. Anoctamin-1 (Ano1), a calcium activated chloride channel is expressed in airway epithelium and its overexpression has been shown to increase cell proliferation. It has also been shown that chloride channels activation can regulate either cell proliferation or apoptosis. However, it was unclear whether Ano1 is expressed in pulmonary vascular endothelial cells (PVEC). We have shown that Ano1 is expressed in the endothelium of pulmonary vasculature and its activation results in reduced cell counts. We hypothesize that Ano1 activation may induce apoptosis of PVEC. To test our hypothesis, rat lung microvascular endothelial cells (RLMVEC) were cultured, treated with Eact, an activator specific to Ano1 and analyzed the resulting responses through cell count, DAPI (4', 6-diamidino-2- phenylindole) stain, and western blotting of apoptotic cell signaling proteins. Ano1 activation with Eact results in increased in RLMVEC apoptosis assessed by the DAPI images, and in increase in p38 phosphorylation, which is attenuated by SB (p38 inhibitor), DIDS (chloride channels inhibitor) and T16A (Ano1 inhibitor). We further expect to see an increase in cleaved Caspase-3 and Bcl-2 expression. We anticipate that our findings on the role of Ano1 in PVEC apoptosis may elucidate a novel target for treating PAH.

Neuroscience
Electrical Conditioning of the Chronic Dopamine Microelectrode for Fast-scan Cyclic Voltammetry

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David P. Daberkow

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This research project addresses the question of what amount of time, of electrical conditioning treatment, would improve sensitivity of the chronic silica encased CFM. Clark et al. in 2010 developed this electrode, which is currently being used to monitor dopamine long-term (weeks to months) in research animals. Fast-scan cyclic voltammetry is a technique used to record dopamine signaling via repeated application potential to the CFM at a frequency of 10 Hz. Increasing the frequency of this applied potential to 60 Hz creates a renewed surface on the CFM (“etching”). This technique has previously been shown to improve the sensitivity of glass encased CFM (Takmakov et al., 2010) used for the acute (hours) monitoring of dopamine. For this project, electrical conditioning was done at time intervals of 0, 15, 30 and 60 minutes. Before and after each etching, sensitivity of the CFM was assessed by monitoring the current response of 1 micromolar dopamine solution in vitro. Dopamine current responses, background currents, and noise levels were recorded. The results from this project indicate a significant improvement in the sensitivity of CFM etched for 30 and 60 minutes (p ≤ 0.05). Results also suggest a trend in stabilization of background current at 30 and 60 minutes, with no statistical significance. This data suggests electrical conditioning at 60 Hz for 30 minutes will significantly improve the sensitivity of the chronic dopamine CFM. With our findings we seek to promote and improve the use of chronic silica encased CFM for in vivo monitoring of dopamine.
Organophosphate pesticides (OPs) such as methyl parathion (MeP) are the most widely used insecticides in the world (Hreljac et al., 2008). OPs are typically esters, amides or thiol derivatives of phosphoric, phosphonic or phosphinic acids (Balali-Mood and Balali-Mood, 2008). Due to their widespread use, a large number of poisonings occur every year in occupationally exposed human populations, and in the general population through the consumption of contaminated food and drinking water (Marrs, 1993 and Yasmashita et al., 1997). The oxon is the mediator of acute OPs toxicity due to its ability to inhibit acetyl cholinesterase activity in the nervous system and neuromuscular junctions. Recent studies have revealed several other targets of OPs, such as MeP that disturb noncholinergic biological systems. For example, the lab has demonstrated locomotor, and neurochemical impairments in the brains of mice after the administration of MeP. However, the neurotoxic effects of MeP on specific brain regions have not been explored. In the present study, we will determine if brain regions have different vulnerabilities to MeP induced neurotoxicity. Using C57BL6 mouse pups at age Po-P1, we will prepare primary neuron-glia co-cultures from various brain regions. We will assess the neurotoxic effects of MeP in the various co-cultures by assessing cytotoxicity, mitochondrial toxicity, reactive oxygen species production, and GPx activity. The findings from these studies will provide insight into the vulnerabilities of various brain regions to MeP induced neurotoxicity, and possibly raise the awareness of the potential neurotoxic outcomes after exposure to MeP.
Drug delivery systems (DDS) are designed to achieve prolonged therapeutic effect with continuous release of the drug in efficient amounts within an acceptable period of time and without loss of its therapeutic activity. Since 1980s, silica and porous materials have been used as promising drug hosting systems and carriers for a variety of drugs.

Zeolites, a particular porous material used as carrier for anthelmintic drugs, were demonstrated to be a slow-release carrier. Having stable 3-D structure, high surface areas with variable channels, cavities and pore sizes, zeolites can also be tailored to suit the need of drug delivery. Additionally, its cavity's size permits relatively easy movement of drugs, facilitating the release of guest molecules from the cavities through openings and channels.

The encapsulation of paracetamol in Zeolite-HY by diffusion in liquid phase, and its efficiency release under simulated body conditions at various pHs (4, 7, and 9 to mimic the stomach, human body, and small intestine, respectively) was investigated.

The amount of paracetamol loading was determined through thermogravimetric analysis. Additionally, scanning electron and transmission microscopic images (SEM, TEM) show that paracetamol was effectively encapsulated into Zeolite-supercages and no changes occur in the morphology and structure upon encapsulation of the drug. In addition to the presence of characteristic drug peaks reflected in the FT-IR spectra, the aforementioned studies on the zeolite encapsulated drug demonstrate that this DDS can be used effectively for sustained release applications. Further in-depth study on this DDS can be conducted and tested under more diverse conditions.

Cocaine is an abused psychostimulant that disrupts mesocorticolimbic circuitry. Females are shown to be more vulnerable to the effects of cocaine when compared to males, requiring lower doses and less exposure time before the onset of addiction. Taurine is an organic acid that has been shown to play neuroprotective and neuromodulatory roles. The objective of the present study is to determine if taurine reduces cocaine preference in male and female subjects. Male and female rats were pretreated with taurine (pre-tau; 100mg/kg; intraperitoneal) for two weeks before undergoing a ten-day conditioned place-preference (CPP) behavioral protocol. They were randomly divided into four groups (n=9/group): (1) taurine-pretreatment (pre-tau) and taurine (tau)+cocaine (coc) co-administration during conditioning, (1) pre-tau and cocaine during conditioning, (3) pre-tau and tau during conditioning, and (4) coc during conditioning. Males and females that were not pre-treated with taurine showed a significant preference to the cocaine-paired chamber. Neither male nor female subjects showed a preference to the taurine-paired chamber, showing taurine is not rewarding. Taurine pretreatment was effective in inhibiting cocaine preference in both male and female subjects; however, females show significant preference towards the cocaine-paired chamber when taurine and cocaine are co-administered. Addiction-induced behaviors often persist for years after abstinence and the best form of treatment is yet to be determined. This study provides evidence that taurine should be studied as a treatment for cocaine addiction; however, sex may influence its efficacy. Further studies will investigate the mechanism by which taurine inhibits cocaine preference and its relationship to gonadal hormones.
Pharmacology and Physiology

**Novel Drug Sources Found at Hydrothermal Vents**

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Deep-sea hydrothermal vents are novel sources for natural products, and the discovered bioactive compounds found within the vents are attributed to the abundance and diversity of microbial communities. Specifically, the chemolithoautotrophic bacteria such as *Phorcysia thermohydrogenphilia* produce secondary metabolites with potential therapeutic applications. *P. thermohydrogenphilia*, a nitrate-ammonifying bacterium, was isolated from a hydrothermal vent on the East Pacific Rise, and was anaerobically cultured to examine the bioactivity of the associated secondary metabolites. The crude organic extract was tested for necrosis activity using a necrosis assay that resembles a MTT assay. One of four isolated fractions expressed necrosis activity. The bioactive fraction was fractionated via RP-HPLC revealing at least seven compounds. Elucidated bioactive compounds will represent novel chemical structures with potential therapeutic applications. Byproducts produced by hydrothermal vent microbial communities are promising medicinal agents, and we are continuously examining fauna associated with hydrothermal vents as novel drug sources.

Pharmacology and Physiology

**Mediators of Acidosis-induced Vasodilation in Renal and Mesenteric Arteries**

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Different mechanisms have been proposed regarding the effects of acidosis on the vasculature depending on the vascular bed studied. The proton-sensing G protein-coupled receptor, GPR4, is part of a family of receptors that help detect pH in blood vessels, bone, kidney, and lungs. We investigated the role of nitric oxide (NO), prostaglandins, endothelium, and GPR4 as mediators of the vascular response to acidosis in two circulations: mesenteric and renal. Male Sprague-Dawley rats, male C57Bl/6 and GPR4-/- mice were euthanized prior to mesenteric and renal artery excision. Four segments per circulation per animal were mounted in individual myograph chambers. In basal tone, phenylephrine concentration response curves were performed at pH 7.0 and pH 7.5. In arteries pre-constricted with phenylephrine, acidosis was induced by gradual addition of HCl to the chambers. L-NAME and indomethacin were used to block NO or prostaglandins production, respectively. Our results showed that in pre-constricted rat renal and mesenteric arteries acidosis induced complete vasodilatation, which was attenuated when pre-incubated with L-NAME. In mice renal arteries, L-NAME treatment or endothelium denudation attenuated acidosis-induced relaxation. Wild type mice arteries experienced attenuated maximal response and sensitivity to phenylephrine, whereas in GPR4-/- arteries sensitivity was lower. The sensitivity of the acidosis-dependent relaxation in GPR4-/- mice renal arteries was attenuated. We concluded that the observed decreased vascular response to phenylephrine in acidosis may mediate functional sympatholysis. Also, endothelium-derived NO appears essential in mediating acidosis-induced vasodilation in small resistance arteries. Lastly, GPR4 partially mediates vasodilatory responses to acidosis in mice renal arteries.
Acetonitrile is a Volatile Organic Compound of modest toxicity widely used in the pharmaceutical industry. It is important to detect and quantify the presence of these compounds to prevent industrial accidents and environmental damage. Acetonitrile is also known to damage animal cell membranes, death or the blood condition methemoglobinemia. In 2012 researchers of North Carolina Agricultural and Technical State University reported the synthesis of Tungstate host which could act as a tunable white light nanophosphor. In the paper “Tunable white light-emission of a CaW_{1-x}Mo_{x}O_{4}:Tm^{3+}, Tb^{3+}, Eu^{3+} phosphor prepared by a Pechini sol-gel method Zerihun Assefa, Matthew Mickens and Dhananjay Kumar reported the crystal structure of their compound possessed vacuum sites which could contain guest molecules. The aim of this study was to test the potential of the tungstate host to be incorporated in a passive sensor of Acetonitrile. To determine the usability of the host, changes in the luminescence profile and crystal structure was examined. Laser spectroscopy was performed using a Surelite Continuum 1064 nm Dye laser, McPherson Model 2035 Monochromator and a Photon Technology International Spectrofluorometer were used to obtain emission/excitation spectra at lower ranges. Crystal structure was studied using an X-ray Diffractometer. Examination of diffractometer plots showed no significant crystal changes in the host due to exposure. Significant changes were observed in the luminescence profiles. After exposure excitation wavelengths experienced a red shift of 6 nm which is a significant enough change to use the material in a sensor.
**Chemistry**

**Application of the Vibrational Spectroscopy for Monitoring the Enzymatic Hydrolysis of Soy Hull**

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Application of the vibrational spectroscopy for monitoring the enzymatic hydrolysis of soy hull. Soyhull is a biodegradable waste that can be used to produce glucose which can be fermented to produce ethanol. An enzymatic treatment with suitable pretreatments to disrupt the structure of the soy hull is examined. Raman spectroscopy was used to monitor the glucose production by enzymatic hydrolysis of the soy hull. Glucose, fructose and sucrose show very similar Raman spectra with characteristic vibration between 1000-1200 cm$^{-1}$. Raman spectral data showed significant changes in peak intensities for concentrations between 0.2 M and 2M of fructose and sucrose solutions. In the case of glucose, changes in peak intensities did not reflect the changes in concentrations, probability due to intermolecular interaction and hydrogen bonding that may play a significant role in the vibrational spectra of glucose. However, Raman spectral data clearly showed the progress of the enzymatic hydrolysis of soy hull. Cellulases from Aspergillus niger and Trichoderma reesei were used for the enzymatic hydrolysis of soy hull and the reactions were monitored for 5 days using peak intensity of characteristic vibration. At the experimental conditions used, there was no significant sugar production observed until 3rd day of hydrolysis. Maximum concentration of sugar observed on 4th day with a decrease in concentration thereafter. This decrease may be result of concomitant fermentation in the medium at later days of the experiment. This study shows that Raman Spectroscopy can be used to monitor cellulosic hydrolysis of waste products such as soyhull.

**Chemistry**

**Alteration of Rare Earth Element Distribution as a Result of Microbial Activity and Empirical Methane Injection**

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Nicholas W. Davies,  
Brian A. Haley,  
Andrew R. Thurber,  
Frederick S. Colwell

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University of California, Santa Cruz, Santa Cruz, CA; Whitman College, Walla Walla, WA

While methane is a potent greenhouse gas, microbial oxidation of methane within the sediment greatly limits the role of marine methane sources on atmospheric forcing. Rare earth elements (REEs) are not currently thought to be involved with microbial activity, but this assumption has not been rigorously tested. Here we test that microbial communities will rapidly respond to the onset of methane emission, and the microbial response to this methane input will impact the distribution of REEs within the sediment. Undisturbed cores sampled from a tidal flat at Yaquina Bay, OR, were brought back to a lab and injected with anoxic seawater (as a control) or anoxic sea water saturated with methane gas for 2 weeks. Aerobic methanotrophs proliferated over this time period, becoming an abundant member of the microbial community. The experimental injection of methane also shifted the distribution of REEs within the sediment, a trend that appeared to follow the microbial response and that was different from the control cores. Further, the lightest REEs appeared to be used more than the heavier ones, supporting that REEs are being actively used by the microbes. While we focused on identifying the response of those microbes responsible in methane-cycling, we also identified how the entire microbial community shifts, and correlating with shifts in REE distribution. Here we have empirically demonstrated the rapid response of methanotrophs to the onset of methane emission and that REE distribution within the sediment is likely impacted by microbial activity, including that involved with methane cycling.
Formation of biomolecules during the prebiotic era is presumed to have taken place before formation of the ozone layer around the Earth’s atmosphere. Formamide has been suggested to have been prevalent on prebiotic Earth because of its low volatility. It has the H, C, N, and O atoms found in organic compounds, and it has been proposed as a precursor for many biomolecules. The primary objective of this project is to determine how biomolecules are formed under mild prebiotic conditions. The reactions were based on formation of biomolecules in a water-pond scenario. Formamide and water were placed under the simultaneous UV irradiation and heat for 48 hours followed by GC/MS analysis. The results show that urea is the major project. Nucleobases can be formed from neat formamide, however, introducing water in the reaction medium prevents the formation of nucleobases and leads to the urea pathway. Urea is prebiotically important because it is a precursor to nucleobases and triazines. Our results demonstrate that the origin of urea is aqueous formamide. The reaction conditions simulate an aqueous pond scenario for formation of urea with the sun as the source of both light and heat.
Regioselectivity in Adjacent Dinitration of Substituted Benzenes

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1,4-Dihalo-2,3-dinitrobenzenes have been synthesized from corresponding p-dihalobenzenes in mixed acids at low temperature. Maximum yields were obtained with optimized conditions for each halo group. The importance of electrophilic aromatic nitration as an industrial process cannot be overstated. Nitroaromatics continue to be indispensable intermediates in synthetic applications ranging from pharmaceuticals to explosives. Nitro-activated aryl halides are precursors to biaryl compounds which constitute the cornerstone of pharmaceutical industry, either through the century old Ullmann coupling or the more recent C-H functionalization methods. Nitration at ortho position to the ring’s halo group(s), hereto referred as selective ortho-nitration, has been anything but selective and literature has no record of examples of adjacent dinitration of aryl dihalides. The mechanism of this reaction has been extensively investigated but is still the subject of animated discussion. Selectivity of the electrophilic aromatic nitration has been intriguing and difficult to predict. Attempts to rationalize the results are still a source of disagreement. Upon examination of several para-substituted aryl dichlorides, dibromides and diiodides using slightly similar nitration conditions, we report on the preparation of several ortho-dinitrated aryl dihalides.

Effect of Soil Application of Trace-elements and Chelating Agent Citric Acid on Soybean Seed Minerals

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This research determined the effects of soil applications of five compounds (Mn, Cu, Zn, Mo and B) with a chelating agent, citric acid (CA), on soybean plants. It is hypothesized that CA by itself or in combination with these five chemical applications can aid in the uptake or decrease the mineral content of the soybean seeds. Six seeds of soybean cultivar (Bolivar with maturity group V) were grown in a repeated greenhouse experiment. The chemical applications were applied either separately or in combination of the compounds with chelating agent CA to three-week-old soybean plants two times. After application the plants were allowed to grow until harvest maturity. The mature, dried soybean seeds were analyzed for a total of thirteen elements. Five minerals and six chelating agents (CA) with minerals applications were used in this study. Cu, Zn, B, and CA caused increases in that element in the plant. Addition of Mn decreased Na and Fe by 39.0 and 7.5%, Cu decreased Na by 25.5%, and B decreased Na and Cu by 32.7 and 29.8%. A possible compound that can alter seed composition may exist and can be used to select the desirable seed composition constituents. In future research, one may use minerals such as Fe and Ca because they are needed in the human body, and if we find a way to transmit the minerals into the soybean seed and make sure it’s edible for digestion, it can help people who have low Fe and Ca.
Poster Presentations

**131 Chemistry**

**Synthesis and Fluorescent Studies of Coumarin Conjugates of Vitamin E**

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Coumarins are a class of naturally occurring compounds in some plants which provide fragrance and a bitter taste for defence against predators. Coumarins are biologically active in human metabolic pathways, and have potential as novel antioxidant compounds in medicinal chemistry. Antioxidants are important as they may prevent disease-causing degradation of DNA, lipids, and proteins by free radicals. Increasing the antioxidant properties and potentially decreasing the toxicity of coumarin compounds can develop new preventative therapies. Furthermore, the fluorescent properties of coumarins have led to their use as highly sensitive biological probes with applications including thiol detection, protein function and cell structure studies. A series of coumarins bearing different functionalities on the 7-position and a carboxylic acid in the 3-position were activated as benzotriazolides and coupled with different amino acids. The reactions proceeded under mild conditions and were complete in less than 2 hours and the products were easily isolated by acidic work-up followed by filtration. Vitamin E is a lipid soluble non-enzymatic antioxidant and it has been shown that vitamin E-amino acid conjugates have enhanced stability and improved water solubility. We envisaged that coupling our coumarin-amino acid conjugates with vitamin E would provide a series of fluorescent vitamin E analogues, possibly with enhanced anti-oxidant properties. We reported herein the results of these studies.

**132 Chemistry**

**The Influence of Aronia Cultivation Management on the Antioxidant Capacity of Aronia**

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Blessing Aroh,
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Aronia Mitschurinii commonly known as the Black Chokeberry is a fruit bearing woody perennial shrub in the rosacea family. Although the original Aronia Melanocarpa is native to Maryland and was used by Native Americans hundreds years ago, in the past decades it was more popular in Russia, Poland and the United Kingdom, after Russian Scientist breaded it with 25% of Mountain Ashe. Aronia is one of the richest plant sources of phenolic and especially anthocyanins. It’s capability to capture free radical makes it an ideal plant for preventing and even treating diseases like cancer, heart disease, and genetic defects. Recent studies has proven that Aronia contain 5 times more antioxidants than assai berry and 40 times more than tomatoes, making it a future supper berry. The aim of this project is to develop and optimize the horticultural management program for growing Aronia in Maryland, in order to produce the crop with as high as possible antioxidant capacity. Our preliminary study of antioxidant capacity of aronia as a function of bush age, sun-shadow ratio, fertilization and pest management influence significantly the antioxidant capacity. Here we present data of the measurements of total polyphenols, anthocyanin content, total flavonoids, pH, and the ORAC factor of Aronia based on the different levels of nitrogen and potassium treatments, conventional and organic, with or without Azomate additive. We are currently looking also at the effect of bush age on the antioxidant content of the berry and will provide three years comparison of data.
Engaging and Learning Data through Prediction Games: A Climate Change Case

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As ever more data streams are made available via the Web, there are opportunities for developing entertaining activities that motivate people to engage this data and learn about the regarding domain. We propose prediction games, based on the interaction model of fantasy sports, to support such activities. We hypothesize that prediction games in a domain that combines real-time and archival data encourage engagement with data and learning through prediction activities. To validate our hypothesis, we propose a domain-independent prediction engine adaptable to any domain with little to no effort. As a consequence, we also posit that there must be necessary and sufficient abstractions for the design of such prediction engine. Then the primary domain of the proposed project shall be climate change and the regarding data shall be of weather (temperature, wind, etc...). Finally, we plan to evaluate the climate change prediction game to answer the research questions engendered by our main hypothesis.

The Complex Zeros of a Gaussian Random Polynomial

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Let $P_n(z)$, where $z$ is a complex variable, be a polynomial whose coefficients are independent, identically distributed and normalized real Gaussian random variables. Let $\omega$ be any Lebesgue measurable subset of the reals and denote by $v_n(\omega)$ the number of zeros in $\omega$ of $P_n(z)$. In 1943, Kac obtained an explicit intensity function $g_n(x)$ for which the expectation of $v_n(\omega)$ is given explicitly by the integral over $\omega$ of $g_n(x) \, dx$ for each $n > 1$. In 1995, Shepp and Vanderbei extended Kac’s result to the case when $\omega$ is any Lebesgue measurable subset of the complex plane. In this talk, I will consider the case when the coefficients are independent, identically distributed and normalized complex Gaussian random variables and use the method of Shepp and Vanderbei to obtain an explicit intensity function $h_n(z)$ expressed in the simplest term for which the expectation of $v_n(\omega)$ is given explicitly by the integral over $\omega$ of $h_n(z) \, dz$ for each $n > 1$. I will also present numerical computations that demonstrates the behavior of $h_n(z)$ for various values of $n$ and limiting expressions for $h_n(z)$ and the expected number of zeros in disks and sectors of the complex plane.
Investigation of the Long Term Behavior of General Predator-Prey Model with Holling Type II Function

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The Lotka-Volterra systems, also known as the predator-prey systems, are first order, nonlinear differential equations that describe the interactions between two biological species. These models have been wildly applied in ecological system and in economics. The model makes some assumptions about the environment and evolution about the predator and prey populations. In this research, a predator-prey model with Holling type II functional response is studied. This model assumes: (1) the prey grow in Malthusian way with the absent of predation (2) the predation is to reduce the prey’s capita growth rate proportional to the prey and predator populations (3) the predator’s death rate with the absent of prey results in an exponential to decline and (4) the prey’s contribution to the predator’s growth rate. The main purpose of this research is to study the long term behavior of the system by conducting a linear stability analysis about equilibrium points, proving if a limit cycle exists and constructing numerical simulations. We used the Routh-Hurwitz criteria to study the stability analysis of the three equilibrium points for the system. It was found that there exist both stable and unstable regions for the coexistence equilibrium. Then we prove the existence of at least one unique limit cycle under a suitable region. These results extend to previous research by Jitsuro Sugie, Rie Kohno and Rinko Miyazaki with a similar model. Numerical simulation using MATLAB compared the theoretical linear stability analysis of the different regions. Numerically we found stable equilibrium, unstable equilibrium and limit cycles.

Counting Symmetric Fullerenes Patches with 4 Pentagons

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This study examines a method for constructing fullerene patches in the hexagonal tessellation of the plane. We extend a result of Graves and Graves (2013) by producing an exact process for drawing fullerene patches with 4 pentagonal faces embedded in them. Attempts to formulate a closed equation for the number of symmetric patches, up to isomorphism, are shown. These include direct counting by predetermining the placement of two pentagonal faces and noting graphical symmetries that cause overcounting, using the Principle of Inclusion-Exclusion approach and by re coordinatizing our depiction from Coxeter coordinates to Euclidean in order to analytically count the patches within the largest convex polygon interior to all the boundary lines we construct.
Ramsey Game Numbers

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In Ramsey Games, which are inspired by Ramsey Theory, two players take turns coloring edges of a complete graph of size $m$ with their color (blue or red). The first one to create a monochromatic subgraph $H$ in his color wins. The Ramsey Game Number of $H$ (denoted $RG(H)$) is the least $m$ such that in a game with two optimal players, some player (it will be Player I) is guaranteed to win. We investigated how big $m$ has to be for various graphs $H$. We prove (1) If $n$ is greater than or equal to 5, $RG(P_n) = n$, where $P_n$ is the path on $n$ vertices, (2) If $n$ is less than or equal to 5, then $RG(S_n) = 2n - 3$ where $S_n$ is the star graph on $n$ vertices, and (3) If $n$ is greater than 5 then $RG(S_n)$ is less than or equal to $2n - 4$ where $S_n$ is the star graph on $n$ vertices. A computer program was used to simulate Ramsey Games and obtain these results; however, the final game-playing strategies involved in the proofs are humanly comprehensible.

Robotics in the Home Care Field

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Attempting to provide a solution to the coming increased demand in service for elderly and disabled patients, we attempted to create a robotic system that will handle one of common but dangerous scenario for those patients, that of falling down to a lack of stability. To do this we used a Rethink Robotics Baxter Reserearch Model, along with a Microsoft 360 Kinect, to track patients without requiring them to wear any sensors. We managed to create a fall detection system using the Kinect's 3-D depth Camera, and then have it notify the Baxter to model to prepare to Catch a patient.
This research training project aims at understanding the optics related to a solar energy harvesting device, namely a Solar Oven for home cooking. The goal is to configure a contraption to suit quality and safe cooking at no cost. A box oven that has a concave mirror inside and reflect flaps (secondary mirrors) was designed to (i) focus in a uniform fashion a sufficient amount of sunlight onto the cooking dish, and (ii) to permit the concentrated light to impinge all sides of the cooking dish. The orientation of the secondary mirrors allow control of the generated heat and led to efficient and uniform collection of the rays and directing them onto the cooking zone. Optics model has been derived and ray tracing technique has been used for tracking the focusing process of sunrays onto the cooking zone. Direct and reflected light rays were analyzed to find the amount of irradiation absorbed by the cooking device throughout the day and at a given time during the day. The results include the optimization of mirror angles for maximum light harvesting as well as the expected efficiency for various regions state- and worldwide.
**Cancer Biology**

**Dual Inhibition Of Mcl-1 By The Combination Of Carfilzomib and TG02 In Multiple Myeloma**

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Carfilzomib (Kyprolis®) is an FDA-approved proteasome inhibitor for single-agent use in relapsed/refractory multiple myeloma (MM). We combined carfilzomib with TG02, a multi-kinase inhibitor. Both independently target Mcl-1 and MM cells are dependent on it for survival.

Four different human myeloma cell lines were treated for 24 hours with carfilzomib +/- TG02. Co-treatment resulted in additive apoptosis in all lines. Carfilzomib pulse dosing was performed to mimic pharmacokinetics. Similar activity was observed with continuous and pulse dosing. Activity of the combination was also observed in freshly isolated samples from relapsed/refractory patients. Co-culture with Hs-5 cells protected against combination treatment in three lines, while addition of Hs-5 conditioned medium was protective in RPMI-8226.

We then determined the molecular basis for increased apoptosis. Treated cells were isolated for western blot and RT-qPCR analysis to determine Bcl-2 family protein levels. Carfilzomib treatment caused an increase in NOXA mRNA. TG02 treatment resulted in decreased Mcl-1 protein but not mRNA expression. Mcl-1 loss at the protein level occurs in the presence of carfilzomib, therefore, the effect of TG02 is unlikely due to increased degradation. Mcl-1 translational regulation is a likely mechanism. These data suggest Mcl-1 dual inhibition is active in myeloma and warrants further preclinical testing.

**Novel Protein-Protein Interactions in Bladder Cancer**

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In the United States there are an estimated 73,510 new cases of bladder cancer each year and 14,880 deaths annually. In terms of research dollars per patient, bladder cancer receives the lowest funding of all cancers and scientists have not yet identified targeted therapies. Data from The Cancer Genome Atlas (TCGA) revealed that the most significant focal amplifications in bladder cancer contains the SOX4 gene at chromosome 6p22 while the most significant focal deletion spans cyclin-dependent kinase inhibitor 2A (CDKN2A). SOX4 amplification and CDKN2A homozygous deletion were mutually exclusive, suggesting they may act in the same pathway. In collaboration with the Emory CTD2 Center and the Chemical Biology Discovery Center, we recently discovered novel high-confidences protein-protein (PPI) interactions between SOX4 and CDKN2A via a high-throughput Time-Resolved Fluorescence Resonance Energy Transfer (TR-FRET) screen. We hypothesize that SOX4 sequesters CDKN2A to inhibit G1/S arrest, thereby deregulating cell cycle checkpoints and promoting tumorigenesis. We validated endogenous SOX4 pull-down of CDKN2A in 5637 and HT1376 bladder cancer cell lines compared to a CDKN2A-deleted control cell line. We disrupted the SOX4 gene in SW780 cells using CRISPR-Cas9 and observed reduced proliferation compared to controls. The interaction of SOX4 and CDKN2A suggests a novel tumor promoting activity that is independent of SOX4’s activity as a transcription factor and could implicate SOX4 as an oncogenic driver in bladder cancer. However, the connection between SOX4 overexpression and tumorigenesis has not yet been definitively demonstrated. Our data could provide a rationale for SOX4 as a therapeutic target in bladder cancer.
A major mechanism of metastasis is the epithelial to mesenchymal transition (EMT) in which epithelial cells from the primary site undergo alterations to become more motile and mesenchymal. A canonical marker of this process and subsequently a clinical marker of metastasis is the intermediate filament protein, vimentin. Clinically vimentin expression has been shown for years to correlate with increased metastatic potential and poor patient prognosis across solid tumor types including lung, prostate, and breast cancers. However little is known about how vimentin works to promote the metastatic cascade. Here we use a lung cancer mouse model to study the role of vimentin in metastasis in vivo. This model has LSL-KrasG12D and LKB1fl/fl mutations that are activated in the lungs upon intranasal administration of lentiviral Cre recombinase. By knocking out vimentin in this model we can study how vimentin contributes to lung cancer metastasis. Our findings show that the KrasG12D/LKB1fl/fl/Vim-/- mouse exhibits significantly less metastasis to the lymph nodes as compared with its vimentin wild type counterpart. These knockout mice also exhibit less focal invasion at the primary tumor site. Taken together, our work indicates that vimentin more than a biomarker and is playing an instrumental role in the metastatic cascade.

Orthogonality constrained density functional theory (OCDFT) [F. A. Evangelista, P. Shushkov and J. C. Tully, J. Phys. Chem. A, 2013, 117, 7378] is a variational time-independent approach for the computation of electronic excited states. In this work we extend OCDFT to compute core-excited states and generalize the original formalism to determine multiple excited states. Benchmark computations on a set of 13 small molecules and 40 excited states show that unshifted OCDFT/B3LYP excitation energies have a mean absolute error of 1.0 eV. Contrary to time-dependent DFT, OCDFT excitation energies for first- and second-row elements are computed with near-uniform accuracy. OCDFT core excitation energies are insensitive to the choice of the functional and the amount of Hartree–Fock exchange. We show that OCDFT is a powerful tool for the assignment of X-ray absorption spectra of large molecules by simulating the gas-phase near-edge spectrum of adenine and thymine.
A rhodium-catalyzed asymmetric synthesis of beta-lactones via intramolecular C–H insertion into the ester group of aryldiazoacetates has been developed. The beta-lactones were synthesized in high yields and with high levels of diastereo- and enantioselectivity. Halo and trifluoromethyl substituents at the ortho position of the aryldiazoacetates enhance intramolecular C–H insertions over intermolecular reactions, allowing C–H insertion of even methyl C–H bonds.

3',5'-cAMP and 3',5'-cGMP are well established mammalian second messengers that control pathways such as glycogen metabolism, vasodilation and phototransduction. However, due to the lack of an efficient extraction and quantification method, neither the roles of additional atypical cyclic nucleotides, including cytidine 3',5'-cyclic monophosphate (3',5'-cCMP) and 2',3'-cyclic nucleotide monophosphate (2',3'-cNMPs) in tumorigenesis and stress-response pathway in biological systems, nor proteins involved in 3',5'-cCMP pathways have been validated. A sensitive and versatile method to extract and quantify multiple cNMPs using LC-MS/MS in mammalian tissues and cellular systems has been developed. This method allows for quantification of multiple cNMPs in complex biological systems, which will aid in identifying their roles in vivo. A panel of rat organs was chosen to establish tissue distribution of eight cNMPs in major rat organ studies. The ability to analyze eight cNMPs simultaneously in a single run demonstrates the efficiency of the developed method. Problems, such as matrix effects from complex biological samples, were addressed and optimized. The study reports the first identification of the potential signaling molecule 2',3'-cIMP and the first quantification of 3',5'-cIMP in mammalian organs, laying the groundwork for future studies of the biochemistry and physiology of both 2',3'- and 3',5'-cNMP isomers.
The influenza A hemagglutinin (HA) viral protein undergoes a dramatic pH driven conformational rearrangement to allow for insertion of its fusion peptide into the host membrane, ultimately leading to membrane fusion between the virus and host, a process critical to the mechanism of influenza infectivity. In this study, we examine the fundamental protein-protein and membrane-protein interactions that HA requires in order to accomplish viral fusion with the host membrane. We probe the mechanism of HA refolding and membrane fusion by interrogating two peptides derived from the HA ectodomain: Loop 40 (L40) the pH sensitive peptide that triggers HA refolding, and the Fusion Peptide (FP), responsible for anchoring HA in the host membrane. Herein, we establish a methodology for studying the dynamics of peptide insertion and membrane fusion by probing the molecular structure of the peptides by infrared spectroscopy. In addition, the L40 peptide refolding dynamics were studied by temperature-jump infrared spectroscopy. Probing the HA folding dynamics with these methods has allowed us to resolve structural dynamics of critical HA components in the sub-millisecond time regime, a time scale inaccessible by other experimental methods currently used to study the mechanism of HA. Together, these results contribute to the mechanistic understanding of influenza viral-mediated membrane fusion by helping to provide a dynamic picture of HA folding and fusion.

To realize the full potential of mobile crowd sensing, techniques are needed to deal with uncertainty in participant locations and trajectories. We propose a novel model for spatial task assignment in mobile crowd sensing that uses a dynamic and adaptive data driven scheme to assign moving participants with uncertain trajectories to sensing tasks, in a near-optimal manner.

Our scheme is based on building a mobility model from publicly available trajectory history and estimating posterior location values using noisy/uncertain measurements upon which initial tasking assignments are made. These assignments may be refined locally (using exact information) and used by participants to steer their future data collection, which completes the feedback loop. We present the design of our proposed approach with rationale to suggest its value in effective mobile crowd sensing task assignment in the presence of uncertain trajectories.
Tetramer and functional avidity measurements have been widely used surrogate measures of T cell receptor (TCR) affinity for antigen in polyclonal T cell responses but a direct comparison to TCR affinity has not been carried out. Using the mouse Lymphocytic Choriomeningitis virus infection model splenic CD4+ T cell responses to GP66-77:I-Ab were assessed for TCR affinity, tetramer avidity and functional avidity (IFN gamma) at multiple time points of acute Armstrong and chronic CL13 infections. The 2D micropipette adhesion frequency assay (2D) was used to assess TCR affinity at the single cell level making polyclonal measurements possible. In each infection high and low affinity cells were observed and the mean 2D affinity decreased from peak infection to later time points. Despite the difference in antigen exposure no significant difference was seen between CL13 and Armstrong mean affinities at the multiple time points we tested. In contrast in the Armstrong infection as antigen is cleared transition from effector to memory resulted in a progressive increase in functional avidity. In CL13 functional avidity sequentially decreased as chronic antigen exposure resulted in sustained PD-1 expression and T cell exhaustion. Disparities were also observed comparing 2D affinity to tetramer avidity. Regardless of decreasing mean affinities tetramer avidity remained the same in each infection and despite similar affinities between CL13 and Armstrong tetramer avidity was higher in the CL13 response. Furthermore tetramer identified only a fraction of antigen specific cells as 2D detected frequency was 2-3 fold more than tetramer at all time points in both infections. A lack of correlation between the three measurements indicates functional and tetramer avidities do not equate to affinity in a polyclonal response and can be modulated without altering the affinity distribution of polyclonal antigen specific cells.
Poster Presentations (EMORY PRESENTERS)

34 Immunology and Molecular Pathogenesis
Generation of a Mouse Model to Study the Role of Tn Antigen in Tumor Biology

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The Tn antigen is a pan-carcinoma antigen that is expressed on 50–90% of carcinomas, including colorectal cancer, but not normal tissues or cells. Despite clinical and histological correlation with disease progression, the role for Tn in tumor biology is unknown. Tn is a truncated mucin-type O-glycan that is normally extended by a glycosyltransferase called the T-synthase, which requires a unique molecular chaperone Cosmc to be properly folded and become active. Defects in Cosmc have been observed in tumor cells and tissue, resulting in loss of T-synthase activity and expression of the Tn antigen. To investigate the role of Tn antigen in colorectal carcinoma, we engineered expression of the Tn antigen in the gut by deleting Cosmc in intestinal epithelial cells (IECs). IEC-Cosmc-KO mice robustly express Tn antigen throughout the GI-tract and, remarkably, develop progressive invasive adenocarcinoma. This is the first in vivo evidence that Tn expression can result in spontaneous colorectal cancer initiation.

* Contributed equally

35 Molecular and Systems Pharmacology
Improving Brain Tumor Surgery with Advanced Imaging Technology

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Glioblastoma (GBM) resection based on contrast-enhanced MRI (CE-MRI) results in a high rate of local recurrence as infiltrating tumor is known to extend beyond enhancement. Metabolic maps from MR spectroscopic imaging (MRSI) have been shown to identify high-risk infiltration zones. Coupling MRSI with fluorescence-guided surgery (FGS) using 5-aminolevulinic acid (5-ALA) may further enhance the degree of tumor resection. In a cohort of GBM patients receiving FGS, 3D MRSI was performed to give full-brain metabolite maps for intraoperative neuronavigation. Tissue was collected from regions with elevated choline/NAA values within and outside of CE regions before tumor debulking. Fluorescence intensity was quantified ex vivo using a hand-held spectrometer. Histopathology slides were analyzed for tissue infiltration using automated image analysis techniques. Choline/NAA shows positive linear trends with the number of tumor nuclei and the presence of ex vivo fluorescence within tissue samples. The trends that Cho/NAA exhibits with histopathology and intraoperative fluorescence of tumor tissue outside of CE-MRI regions support its use for identifying tumor infiltration. This is the first time that 5-ALA fluorescence has been shown to correlate with MRSI-derived metabolic markers, and we believe the combination of MRSI-neuronavigation with FGS will result in more complete GBM resections and increased patient survival.
Expression of a Gq-coupled Dreadd (Designer Receptor Exclusively Activated by Designer Drugs) in the Rat Prefrontal Cortex

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The nucleus accumbens (NAc) is a region in the brain widely believed to be crucial for relapse-like behavior, particularly cocaine-primed reinstatement in rats. While cocaine is known to elevate norepinephrine, dopamine and serotonin, glutamate release is also augmented in the NAc following a cocaine prime and is required for drug-seeking behavior. While many neuronal sources of glutamate innervate the NAc, pyramidal cells originating in the dorsal prefrontal cortex (dPFC) are particularly critical for cocaine-primed reinstatement. DREADDs (designer receptors exclusively activated by designer drugs) are engineered muscarinic acetylcholine receptors that no longer respond to acetylcholine but can be activated by the synthetic ligand clozapine-N-oxide (CNO). To further explore the functional neuroanatomy underlying drug seeking, we infused adeno-associated virus encoding hM3Dq, a Gq-coupled DREADD, into the dPFC of rats. We found that viral injection was robust after one month and induced c-Fos expression upon CNO challenge. In the future, these DREADD-expressing animals will be subjected to cocaine self-administration followed by abstinence, and we predict that CNO administration will activate the dPFC neurons projecting to the NAc and trigger relapse-like behavior.

Insulin-like Growth Factor-1 Receptor Signaling Increases the Invasive Potential of HER2-overexpressing Breast Cancer Cells via Src-FAK and FoxM1

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Resistance to HER2-targeted antibody trastuzumab is a major clinical concern in the treatment of HER2-positive breast cancer. Increased expression or signaling from the insulin-like growth factor-1 receptor (IGF-1R) has been associated with trastuzumab resistance. However, the specific mechanisms through which IGF-1R promotes resistance remain poorly defined. In this study, we found that IGF-1R crosstalk to HER2 requires Src kinase activity, and that Src regulates FAK phosphorylation in resistant cells. Further, we showed that the major biological effect induced by IGF-1 was cellular invasion, which was mediated by both Src-FAK and the transcription factor FoxM1. Pharmacological inhibition of IGF-1R in combination with trastuzumab suppressed the invasiveness of trastuzumab-resistant cells and also induced antibody-dependent cellular toxicity. Further, we showed that the major biological effect induced by IGF-1 was cellular invasion, which was mediated by both Src-FAK and the transcription factor FoxM1. Pharmacological inhibition of IGF-1R in combination with trastuzumab suppressed the invasiveness of trastuzumab-resistant cells and also induced antibody-dependent cellular toxicity. Further, knockdown of IGF-1R plus trastuzumab down-regulated FoxM1 expression, and inhibited cellular invasion. Finally, we found that FoxM1 contributed to IGF-1-stimulated invasion of trastuzumab-resistant cells, such that knockdown of FoxM1 rescued IGF-1-mediated invasion, whereas re-expression of FoxM1 restored the invasive potential of IGF-1R knockdown cells treated with trastuzumab. Overall, our results indicate that therapeutic combinations that co-target IGF-1R and HER2 may reduce the invasive potential of trastuzumab-resistant cells, and that these anti-invasive effects are due, at least in part, to inhibition of Src-FAK and FoxM1.
Mutations in cilia genes cause abnormal Sonic hedgehog (Shh) signaling and a class of diseases called ciliopathies. The cilia gene Arl13b has been linked to the ciliopathy Joubert Syndrome (JS), which causes intellectual disability, movement disorders, and abnormal development of the hindbrain. JS patients also show classic signs of abnormal Shh signaling in craniofacial and limb development, consistent with the fact that canonical Shh signaling requires an intact primary cilium.

“Non-canonical Shh signaling” refers to downstream effects of Shh that require Shh receptors and effectors, but do not require cilia or gene transcription. These effects include cytoskeletal rearrangements important for axon pathfinding and cell migration. In addition to classic canonical Shh defects, JS patients exhibit abnormal axon guidance and neuronal migration, but the relationship between these phenotypes and the Shh pathway is not known.

I hypothesized that 1) mutations in Arl13b can affect non-canonical Shh signaling, and 2) the disruption of cilia-related genes important for non-canonical Shh signaling contributes to ciliopathy phenotypes. To test my hypotheses, I deleted Arl13b in cell types that are known to exhibit non-canonical Shh signaling. This caused impaired Shh-dependent migration in Arl13b null fibroblasts in vitro, and neuronal phenotypes consistent with JS in vivo. I tested the effect of Arl13b mutations on canonical and non-canonical Shh signaling and saw that JS-causing alleles fail to rescue the Arl13b null phenotype. Surprisingly, a mutation that prevents cilia localization of Arl13b also fails to rescue Shh-dependent migration in fibroblasts. Therefore, while the cilia itself is dispensable for non-canonical Shh signaling, cilia-associated proteins still affect the pathway, and non-canonical Shh defects may contribute to human ciliopathies.

Mutations in cilia genes cause abnormal Sonic hedgehog (Shh) signaling and a class of diseases called ciliopathies. The cilia gene Arl13b has been linked to the ciliopathy Joubert Syndrome (JS), which causes intellectual disability, movement disorders, and abnormal development of the hindbrain. JS patients also show classic signs of abnormal Shh signaling in craniofacial and limb development, consistent with the fact that canonical Shh signaling requires an intact primary cilium.

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Projections of the Cerebellar Nuclei in Bengalese Finches

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The cerebellum is involved in motor skills, but its role in vocal motor behavior remains unclear. Songbirds provide a model system for vocal learning, but it is unknown if the cerebellum is involved in birdsong or if a direct route exists from the cerebellum to the song system, the network of brain nuclei required for song learning and production. Using standard tract-tracing methods, we show that a wide region of the cerebellar nuclei (CbN) projects to the dorsal thalamus in songbirds. Initial results suggest a topography, where more lateral parts of CbN project to more lateral parts of dorsal thalamus. We also found that injections of retrograde tracer into the basal ganglia nucleus of the song system, Area X, labeled dorsal thalamic cell bodies close to fibers labeled by injections of anterograde tracer into CbN. This is consistent with previous work (Person et al 2008) but may be confounded by tracer uptake by fibers of passage. Experiments in progress use anterograde tracers to show whether dorsal thalamus actually projects to the basal ganglia. Lastly we find that some injections in dorsal thalamus label forebrain areas outside the song system, suggesting multiple pathways from the cerebellum to the forebrain in birds.

A New Step in Ciliogenesis: The ANO1 Nimbus

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Many cells possess a single, non-motile, primary cilium that is thought to be a sensory transducer akin to a cellular antenna. Ciliogenesis involves migration of the basal body to the cell surface followed by outgrowth of the axoneme by intraflagellar transport. We have previously identified an early step in cilium development, the formation of a novel structure - the nimbus. Prior to cilium extension, ANO1, a Ca2+-activated Cl- channel and other ciliary proteins including the small GTPases CDC42 and Arl13b, exocyst complex components, and acetylated α-tubulin and β-tubulin are organized into this torus-shaped structure. This structure forms an interface between the microtubule cytoskeleton of the nascent cilium and the surrounding cortical actin cytoskeleton. During ciliogenesis, the nimbus disassembles and ciliary components, including ANO1, move into the cilium. Recently, we have found that the nimbus contains a high concentration of poly-A RNA and is potentially a site of local protein synthesis. Our data support a model where the nimbus is a staging area for assembly of ciliary components and cilia assembly and suggests that local protein synthesis plays a role in the early stages of ciliogenesis.
Biochemistry, Cell and Developmental Biology  
**The Role of Anoctamins in Phospholipid Scrambling and Human Disease**

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The loss of phospholipid asymmetry at the plasma membrane functions as a tightly regulated signaling mechanism ubiquitous in eukaryotic cells. This lipid rearrangement known as phospholipid scrambling (PLS) is an important regulator of apoptotic signaling and cellular fusion but little is understood about the mechanism underpinning this process. Moreover, dysfunction of PLS results in human genetic disease and has been recently identified as a common property of human cancer lines, underscoring the merit in further characterizing the process.

Here we have combined patch clamp recording with simultaneous confocal microscopy to study the role of the putative chloride channel, anoctamin 6, in PLS. We show that ANO6 elicits robust Ca2+-dependent PLS, that this activity coincides with non-specific ionic currents uncharacteristic of other anoctamins and identify a domain in ANO6 that is both essential for these functions and sufficient to convey these activities to other anoctamins. Additionally, we characterize the role of ANO5 in PLS and investigate how the loss of function of ANO5 leads to congenital myopathies. These findings provide a mechanistic framework for understanding PLS and how ANOs 5 and 6 function in this process.

Biostatistics  
**Statistical Approaches for Exploring Brain Connectivity with Multi-Modal Neuroimaging Data**

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By combining various types of neuroimaging data, multimodal imaging analyses enable us to study the relationship between brain structure and function, and investigate the connectivity disruption pathways that characterize certain brain diseases. We develop a novel measure, sSC, to quantify the strength of structural connectivity (SC) underlying functional networks identified using data-driven methods such as independent component analysis (ICA). The sSC statistic can be defined on both the voxel- or region-level using diffusion tensor tractography. We provide a framework to conduct statistical inference for sSC, which overcomes many computational challenges due to spatial correlations within the data and the estimation of a large variance-covariance matrix. We will discuss our estimation methods and illustrate the application using an fMRI dataset.
Human brains perform tasks via complex functional networks consisting of separated brain regions. A popular approach to characterize brain functional networks in fMRI studies is independent component analysis (ICA), which is a powerful method to reconstruct latent source signals from their linear mixtures. An important goal in many fMRI studies is to investigate how clinical and demographic variables affect brain functional networks. Existing ICA methods, however, cannot directly incorporate these covariate effects in ICA decomposition. Hence, researchers can only address this need via heuristic post-ICA analyses which may be inaccurate and inefficient. In this paper, we propose a hierarchical covariate ICA (hc-ICA) model that provides a formal statistical framework for estimating and testing covariate effects in ICA. To obtain the maximum likelihood estimates of hc-ICA, we first present an exact EM algorithm with analytically tractable E-step and M-step. We then develop a subspace-based approximate EM that can significantly reduce computation time while retaining high estimation accuracy. To test covariate effects on functional networks, we introduce a voxel-wise approximate EM that can significantly reduce computation time while retaining high estimation accuracy. We demonstrate the advantages of our methods over the existing method via simulation studies. The proposed hc-ICA is applied to an fMRI study to examine the effects of Zen meditation practice on brain functional networks. The results show that meditators demonstrate better synergy or functional connectivity in several relevant brain functional networks as compared with the control. These findings were not revealed in previous analyses of this data using existing group ICA methods.

Over the last several decades, the use of halogenated organic compounds has become the cause of environmental and human health concerns. Of particular notoriety has been the establishment of the neurotoxicity of polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs). The subsequent banning of PBDEs has led to greatly increased use of hexabromocyclododecane (HBCD) as a flame retardant in consumer products. The physiochemical similarities between HBCD and PBDEs suggest that HBCD may also be neurotoxic to the dopamine system. The purpose of this study was to assess the neurotoxicity of HBCD on the nigrostriatal dopamine system using an in vitro and in vivo approach. We demonstrate that HBCD causes significant cell death in a dopaminergic cell line, as well as reductions in the growth of TH+ primary cultured neurons. Assessment of the in vivo neurotoxicity of HBCD resulted in significant reductions in the expression of the striatal dopamine transporter (DAT) and VMAT2, both of which are integral in mediating dopamine homeostasis and neurotransmission in the dopamine circuit. However, no changes were seen in the expression of TH in the dopamine terminal, or striatal levels of dopamine. To date, these are the first data to demonstrate that exposure to HBCD disrupts the nigrostriatal dopamine system. Given these results and the ubiquitous nature of HBCD in the environment, its possible role as an environmental risk factor for Parkinson disease should be further investigated.
Prenatal maternal stress has been shown to have an adverse effect on pregnancy outcomes such as preterm birth (PTB), which can have lingering effects on a child’s well-being. This analysis explores the potential effect of maternal stress on child academic performance and mediation of this relationship through PTB. The study population comprises 3325 first-grade children born to Georgia-resident mothers between 2000 and 2002 with linkable data on state standardized test performance, birth certificates, and the Pregnancy Risk Factors Assessment Monitoring Survey (PRAMS). Exposures were defined as maternal experience, in the year preceding the birth, of at least three stressful life events (SLE). The intermediate was PTB (<37 weeks gestation), and the outcomes were failure to pass each test section (English Language and Arts [ELA], Math, Reading). Logistic regression indicated partner-related SLEs, maternal education, primiparity, and delivery payor (Medicaid vs. other) as significant predictors (p<0.05) of PTB, while regression on test performance indicated PTB, maternal education, maternal race, delivery payor, and child sex as significant predictors (p<0.05). Mediation analysis using a SAS macro showed a null relationship between SLEs and test performance, also indicating that this relationship was not mediated through PTB (controlled direct effect of SLEs on ELA 1.07 [0.73, 1.55], natural indirect effect 1.01 [0.99, 1.04]). This is consistent with prior research showing a null or weak effect of SLEs on PTB. There was some evidence of effect modification by Medicaid status. Future analyses should explore these relationships in a larger cohort with random sample selection.

Lead (Pb) exposure and body burdens have been widely studied for their neurologic effects such that sufficient evidence exists for widespread acceptance of causality by the majority of the scientific community. At levels well below the acute toxicity point in children, effects such as decreases in IQ scores, increases in attention disorders, and decreases in academic achievement have been observed. Endocrine modulation is a lesser studied potential health outcome of Pb exposure. Pb along with other heavy metals (e.g., arsenic, cadmium) have been hypothesized to alter hormone-regulated activities specifically in critical windows of exposure during pregnancy. Work within a cohort of agricultural working mothers in Northern Thailand will provide information on whether heavy metals are related to hormonal alterations in neonates. This information will be used to prepare educational intervention materials to help inform poor, uneducated Thai women on the potential harm chemical exposures can have on their unborn child.
Epidemiology

Validity and Feasibility of Activity Monitors among Free-Living Elementary Students

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Purpose: To compare steps and time spent in moderate-to-vigorous physical activity (MVPA) reported by two pedometers/activity monitors with a validated accelerometer among fourth grade students under free-living conditions. Ease of use, comfort, level of interference with work and play, overall appeal, and device removal among children was also assessed for the physical (PA) monitoring devices. Methods: Study participants (n=118) wore the Actigraph accelerometer and one of two secondary devices (Fitstep and Pebble) simultaneously during school hours for one week. Daily steps and time spent in MVPA were recorded. Student questionnaires were completed at the end of the week. Results: Fitstep overestimated Actigraph-reported steps by 1,462 steps, while Pebble underestimated Actigraph-reported steps by 962 steps. However, Fitstep- and Pebble-reported steps were significantly correlated with Actigraph-reported steps (r=0.64 and 0.68). Fitstep and Pebble overestimated Actigraph-reported time spent in MVPA by 5.9 and 18.8 minutes respectively. Correlation of time spent in MVPA between Actigraph and Fitstep (r=0.28, p<0.0001) was poor, and correlation of time spent in MVPA between Actigraph and Pebble (r=0.42, p<0.0001) was moderate. Overall ease of use, comfort, and appeal were high, and level of interference with work and play was low. Conclusion: Pedometers/activity monitors can be used in place of the accelerometers to monitor steps if proper user training and device attachment protocols are used.

Epidemiology

Surveillance of the “Missing Half” of Fetal-infant Mortality: Formative Research to Determine the Acceptability of a PRAMS-like Survey among Women Who Have Recently Experienced a Stillbirth

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Roughly one-half of U.S. fetal and infant deaths from 20 weeks’ gestation to one year occur as stillbirths, and stillbirth mortality has not decreased substantially since the 1980s. Since 1987, CDC and state health departments have used the Pregnancy Risk Assessment Monitoring System (PRAMS) to survey women with a recent live birth. Expanding PRAMS to include women with recent stillbirths could provide much-needed surveillance data. Eligible women can be identified through vital records, utilizing methodologies similar to those already employed by PRAMS. It is unknown whether bereaved mothers would be amenable to a PRAMS-like interview and whether the protocol requires modification for this population.

In partnership with CDC’s Division of Reproductive Health, we interviewed stillbirth advocacy leaders (N=10) and women who experienced a recent stillbirth (N=11) to explore whether bereaved mothers would be willing to answer survey questions about their experiences.

Respondents strongly supported the implementation of a PRAMS-like survey for stillbirth, citing both scientific and emotional benefits. While there was no consensus on when to administer the survey relative to the loss, most women thought that waiting 3-4 months post-loss would be appropriate. Some expressed concerns regarding aggressive follow-up during this time of grief.

Given the positive response, CDC will pilot this survey in 2-3 states in the coming year. If successfully implemented, this state-based surveillance system for stillbirth can provide women’s health advocates, public health policy makers, and private healthcare providers with current information to use for healthcare quality improvement leading to a reduction in stillbirths.
Genetics and Molecular Biology

Mechanisms of Drought Stress Memory in Arabidopsis thaliana

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Epigenetic changes are an important mechanism by which organisms can adapt to their surroundings. DNA methylation, small RNA expression, and histone modifications are some of the epigenetic marks that can be passed on through mitotic and meiotic cell divisions. These marks can be reprogrammed in response to environmental stimuli and passed on to newly divided cells, or even to the next generation, as a form of heritable “memory.” Plants are stationary organisms that must constantly respond to a changing environment to survive. Inheritance of a “stress memory” could provide a plant’s offspring with tolerance to stresses specific to their environment, such as drought. Here we show that Arabidopsis thaliana plants can be primed for drought stress by dehydrating the plants for 2 hours at 11 days post germination. The primed plants had increased tolerance to drought stress, even after being grown under control conditions for 2 weeks, compared to non-primed plants. Previous literature related RNA Polymerase II (Pol II) pausing with the short-term (1 day) transcriptional memory of the plants that were primed for drought stress. We are currently testing if Pol II pausing is involved in the long-term stress memory that persists for 2 weeks. Furthermore, we are testing if increased tolerance to drought stress is heritable, and if the Pol II pausing signatures are reestablished in the progeny. Our long-term goals are to identify the transcripts essential for increased drought tolerance by characterizing the regions of the genome where Pol II is pausing in response to drought stress.

Durability of Drug-Induced Reprogramming of the Cancer Epigenome

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Aberrant DNA methylation is a critical feature of cancer. Epigenetic therapy seeks to reverse these changes to restore a normal gene expression profile, diminishing the invasive properties of cancer cells. The DNA demethylating agent 5-Aza-2'-deoxycytidine (DAC) is currently used in the treatment of certain leukemias, and has shown promise in solid tumors when combined with other agents. However, the specific demethylation events that underlie its clinical activity remain unknown. Here, we tracked the DAC-induced genomic demethylation, and subsequent remethylation following drug withdrawal, in triple-negative breast cancer cells to elucidate the factors that underlie the durability of the antitumor response. CpG sites that underwent rapid remethylation had higher pretreatment methylation levels and were enriched in gene bodies and other distal sites, marked by H3K36me3 in normal breast cells, and exhibited hypomethylation in primary breast tumors. In contrast, CpG sites that were resistant to remethylation, were within or near CpG islands, marked by H3K27me3 or H3K4me in normal breast cells, and were often hypermethylated in primary breast tumors. Our data indicate that the selectivity of DAC treatment is twofold: not only are highly methylated areas, especially CpG shores, more prone to demethylation, but tumor-specific hypermethylation is rarely regained.
GNB3 Overexpression Causes Obesity and Metabolic Syndrome

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Duplication of the guanine nucleotide-binding protein beta subunit 3 (GNB3) gene is associated with early-onset obesity. Children with an unbalanced chromosome translocation that includes GNB3 have BMI values above the 95th percentile. A cytosine to thymine (C825T) polymorphism in GNB3 is also associated with hypertension, obesity and metabolic syndrome; however the mechanism of GNB3-related obesity is unknown. We created BAC-transgenic mice that carry the human risk-allele (T) of GNB3. Heterozygous mice express transgenic GNB3 in whole brain, hypothalamus, olfactory bulb, and cerebellum at levels significantly greater than endogenous Gnb3. These GNB3-T mice weigh significantly more than their wild-type littermates starting at age 6-7 weeks (p=0.002). At 20 weeks, GNB3-T mice have greater subcutaneous and visceral white adipose tissue (WAT) and brown adipose tissue (BAT) depots, larger white adipocytes, and larger livers compared to wild-type littermates. Lean mass is the same between GNB3-T and wild-type mice, indicating that the difference in weight is strictly due to an increase in fat mass. Even though GNB3-T mice have greater adiposity, they have similar food intake compared to their wild-type littermates at age 5, 10, 15, 20 and 25 weeks. Fasting plasma ghrelin and PYY levels are similar to wild-types, while amylin is elevated in GNB3-T mice at 20 weeks, suggesting proper satiety. GNB3-T mice have glucose intolerance and higher fasting plasma glucose, insulin, C-peptide at 20 weeks, consistent with type 2 diabetes. GNB3-T mice also have higher fasting plasma leptin, triglycerides, total cholesterol and phospholipids at 20 weeks compared to wild-type littermates. At 20 weeks, GNB3-T mice have difficulty maintaining core body temperature during acute cold stress compared to wild-type littermates. Lep expression is increased in subcutaneous and visceral WAT and BAT in GNB3-T mice, while Ucp1 expression is decreased in subcutaneous WAT. Taken together, these data suggest that GNB3-T mice exhibit obesity and metabolic syndrome. Future experiments will test whether GNB3-T overexpression is associated with changes in activity and heat production.

Understanding the Transcriptional Regulatory Mechanisms of the Histone Variant, H2A.Z, through its Interactions with Chromatin Remodelers

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Differentiating cells acquire a stable transcriptional program necessary for proper development and homeostasis, which is facilitated by chromatin components, such as incorporation of histone variants into nucleosomes. The histone H2A variant, H2A.Z, is involved in many genomic processes, including transcriptional regulation. However, the mechanism through which it regulates transcription is currently unclear. H2A.Z is necessary for transcription of the FLOWERING LOCUS C (FLC) gene in Arabidopsis, but in the absence of transcriptional repressors, such as the chromatin-remodeling component Brahma, H2A.Z is no longer required for transcription of the gene. This project focuses on elucidating the mechanism by which Brahma antagonizes H2A.Z function to infer the role of H2A.Z in transcriptional regulation. We will determine whether Brahma antagonizes H2A.Z-mediated activation at FLC and similarly regulated loci through affecting nucleosome positioning or occupancy and whether H2A.Z localization across the gene is dependent on Brahma. Additionally, we are conducting a forward genetic suppressor screen to identify mutants that alleviate the need for H2A.Z incorporation into nucleosomes for FLC activation. Currently, three candidate lines have been identified as suppressor mutants. Future work to identify and characterize these suppressors will allow us to more thoroughly expand our model of how H2A.Z functions in transcriptional regulation.
Emotional Autobiographical Memories: Event-related Potentials (ERPs) Reveal Differential Neural Processing

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The world is an emotional place. We’re constantly bombarded with emotion (ours and others’) and that influences what we remember. Among adults, there is evidence of differential neural representation of autobiographical memories as a function of emotional valence. Children also seem to show differential neural responses to positive relative to negative autobiographical memories (Bauer et al., 2012). The purpose of the present study was to examine ERPs during retrieval of emotional autobiographical memories, taking into account rated valence and intensity of the memories. Twenty-nine 8-year-old girls participated. Each child used 30 words to elicit memories of 10 emotionally neutral, 10 positive, and 10 negative events used thirty words. Next, we recorded ERP data as the children retrieved the memories again. Neural responses differed as a function of the emotional valence of the events retrieved: positive memories elicited a more negative-going response compared to other memories. The observed pattern supports the interpretation that the effect is due to the valence of the memory, since the effect is also observed for memories that were subsequently coded as matching their valence condition (e.g., memory in the negative condition subsequently coded as containing negative valence). This study adds to the relatively sparse literature on the retrieval of children’s emotional autobiographical memories utilizing ERPs. This work is the first account of school-age girls’ retrieval of emotional autobiographical memories while examining the valence and intensity of their memories and provides a foundation for future research on valence and intensity on the development of autobiographical memory.

Information Transmission by Receptors Correlated through Ligand Diffusion

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Receptors on a cell surface capture external ligand molecules to estimate their concentrations. Due to extrinsic fluctuations in the ligand concentrations, such receptors have positive correlations among themselves. In addition, the discreteness of the ligand molecules and the fact that a single molecule can only be absorbed by one receptor, results in negative correlations among the receptors. This structure of extrinsic and intrinsic correlations is widely expected to increase the information that the receptors measure about the ligand. Here we argue analytically and numerically that these correlations have only a small effect on the information, and the information is, surprisingly, decreased by the correlations.
Schizophrenia and autism spectrum disorders (ASD) are neurodevelopmental disorders that entail social, communicative, and cognitive impairments (Sasson et al., 2011). Increasing evidence indicates a shared etiology (e.g., genetic, prenatal, and environmental risk factors). Few studies, however, have examined ASD within the development of schizophrenia. A prodromal period of functional decline and attenuated psychotic symptoms arises in adolescence and precedes the disorder’s onset (Cannon et al., 2008). It is assumed that there are multiple etiologic subtypes given the complex neuropathogenesis of schizophrenia. A prodromal period of functional decline and attenuated psychotic symptoms arises in adolescence and precedes the disorder’s onset (Cannon et al., 2008).

The present study examined whether clinical high-risk (CHR) individuals with an ASD diagnosis exhibited differences in prodromal symptomatology compared to those without an ASD diagnosis. Twenty-five CHR participants enrolled in the North American Prodrome Longitudinal Study with an ASD diagnosis and were matched to twenty-five CHR participants without ASD. The Structured Interview for Prodromal Symptoms (McGlashan et al., 2001) assessed symptomatology. Multivariate analyses of variance revealed that the ASD group endorsed higher levels of social anhedonia (SA) and less suspiciousness/persecutory ideas than the non-ASD group. Findings regarding elevated levels of SA carry noteworthy implications as individuals high in SA report less social support, more family conflict, and poorer social functioning (Blanchard et al., 2011). Future research should investigate social cognitive deficits as determinants of elevated SA.