EMORY UNIVERSITY — LANEY GRADUATE SCHOOL

STEM RESEARCH AND CAREER SYMPOSIUM

September 18–20, 2016
Emory Conference Center

Diversity in Action
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 2016 Chair and Co-Chair of this event are 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
- Eduardo Sanabria, Graduate Division of Biological and Biomedical Sciences – Molecular and Systems Pharmacology
- Pat Marsteller, Director, Center for Science Education
- Jamie King, Graduate Division of Biological and Biomedical Sciences – Cancer Biology
- Hillary Rodman, Psychology

THE SPONSORS AND PARTICIPANTS:
We extend our gratitude to the many offices, units and programs at Emory 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

We would also like to thank our corporate sponsors AEON Global Health and Kaiser Permanente.
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 115 undergraduate and graduate students from a number of schools beyond Emory, as well as 20 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 September 20th. 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.

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

Lou Ann Brown
Director, Office of Postdoctoral Education, Emory University

Paul Byrnes
Chief Business Officer, Laney Graduate School, Emory University

Anita Corbett
Co-Director, MD/PhD Program, Emory University

Felicia Fullilove
Chemistry and Biochemistry, Spelman College

Triscia Hendrickson
Biology, Morehouse College

Cathryn Johnson
Senior Associate Dean, Laney Graduate School, Emory University

James Kindt
Co-Chair of Organizing Committee, Chemistry, Emory University

Ward Kirlin
Pharmacology and Toxicology, Morehouse School of Medicine

Cora MacBeth
Assistant Dean for Student Affairs, Laney Graduate School, Emory University

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

Tiffany Oliver
Biology, Spelman College

Keith Wilkinson
Graduate Division of Biological and Biomedical Sciences – Biochemistry, Cell and Developmental Biology & Cancer Biology, Emory University

Damon Williams
Director of Diversity, Community and Recruitment, Laney Graduate School, Emory University

Edward Morgan
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Damon Williams
Director of Diversity, Community and Recruitment, Laney Graduate School, Emory University
## Opening Remarks

**Chad R. Jackson, PhD**

is a 2014 – 2016 AAAS Science and Technology Policy Fellow. He is at the U.S. Department of State serving as a Science Policy Advisor in the Office of the Science and Technology Adviser to the Secretary of State. His position stands at the intersection of science and international affairs, working within a wide range of U.S. and international partners to scan the horizon for emerging-transformational technologies and entrepreneurs/innovators that are likely to have significant effects on political and economic landscapes. Dr. Jackson has a wide range of scientific interests that include neuroscience, molecular and cellular biology, robotics, and smart cities technology to name a few. Dr. Jackson’s main goal is to make sure that science and technology are at the forefront of addressing the world’s most critical problems. Dr. Jackson obtained a BA in Biochemistry in 2002 from Earlham College in Richmond, IN and a PhD in Molecular and Systems Pharmacology from Emory University in 2010.

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### Dinner Speaker

**Michael L. Lomax, PhD**

is President and Chief Executive Officer of the United Negro College Fund, the nation’s largest private provider of scholarships and educational support to African Americans. Under his leadership, UNCF has raised $2.3 billion, helping more than 92,000 students earn college degrees and launch careers. Annually, UNCF’s work enables 60,000 students to go to college with UNCF scholarships and attend its 37 member historically black colleges and universities. Before coming to UNCF, Lomax was president of Dillard University and a literature professor at Morehouse and Spelman Colleges. He serves on the boards of Teach For America and the KIPP Foundation. He founded the National Black Arts Festival. Dr. Lomax received his PhD in American and African-American literature from Emory in 1984.

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## Schedule of Events

### All Sunday and Monday events will take place at the Emory Conference Center.

Tuesday’s events will take place at the Emory Conference Center and on the Emory Campus.

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<th>Date</th>
<th>Time</th>
<th>Event</th>
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<td><strong>Sunday, September 18</strong></td>
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<tr>
<td>4:00 – 6:00 pm</td>
<td>Registration</td>
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<td>Great Hearth / Lobby</td>
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<tr>
<td>6:00 – 8:00 pm</td>
<td>Welcome Reception</td>
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<td><strong>Monday, September 19</strong></td>
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<tr>
<td>8:00 – 9:00 am</td>
<td>Registration</td>
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<td>Emory Amphitheatre Foyer</td>
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<td>8:00 – 8:45 am</td>
<td>Continental Breakfast</td>
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<td>Emory Break Area</td>
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<tr>
<td>9:00 – 9:45 am</td>
<td>Keynote Speaker</td>
<td>Chad Jackson, PhD</td>
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<td>10:00 – 11:15 am</td>
<td>Student Oral Presentations 1</td>
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<td>Emory Amphitheatre</td>
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<tr>
<td>11:20 – 11:45 am</td>
<td>Break</td>
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<tr>
<td>11:45 am – 1:00 pm</td>
<td>Poster Session 1</td>
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<td>Lullwater</td>
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<tr>
<td>1:15 – 2:45 pm</td>
<td>Lunch with Emory Program Representatives</td>
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<td>Silverbell</td>
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<tr>
<td>3:00 – 4:15 pm</td>
<td>Poster Session 2</td>
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<td>Lullwater</td>
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<tr>
<td>4:30 – 5:45 pm</td>
<td>Student Oral Presentations 2</td>
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<td>Emory Amphitheatre</td>
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<tr>
<td>6:30 – 8:30 pm</td>
<td>Dinner with Speaker</td>
<td>Michael Lomax, PhD</td>
<td>Salons 1 – 3</td>
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<tr>
<td>9:00 pm – 12:00 am</td>
<td>Social Event (Bowling and Billiards)</td>
<td>Mingle with Emory students, postdocs and faculty</td>
<td>Wisteria Lanes</td>
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<tr>
<td><strong>Tuesday, September 20</strong></td>
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<td>8:00 – 8:45 am</td>
<td>Continental Breakfast</td>
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<td>Cox Hall</td>
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<tr>
<td>9:00 – 9:50 am</td>
<td>Professional Development Breakout Session 4 concurrent</td>
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<td>Cox Hall</td>
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<tr>
<td>10:00 – 10:50 am</td>
<td>Professional Development Breakout Session 4 concurrent</td>
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<td>Cox Hall</td>
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<tr>
<td>11:00 – 12:15 am</td>
<td>Campus Tours</td>
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<tr>
<td>11:15 am – 12:30 pm</td>
<td>Roundtable discussion with Emory faculty for advisors (with lunch)</td>
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<td>Hotel Dining Room</td>
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<tr>
<td>12:30 pm</td>
<td>Lunch and Departure</td>
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Find the table of interest, pick up your lunch, and enjoy.

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DOGWOOD
- Office of Postdoctoral Education
- FIRST
- Minority Postdoc Council
Professional Development Breakout Sessions

Conference rooms are on the third floor.
### Professional Development Breakout Sessions

**September 20 · 9:00 – 9:50 am**

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<tr>
<th>Research Opportunities for Undergraduates at Emory and Beyond</th>
<th>Conversations with Faculty about Graduate School</th>
<th>Life of a Postdoc</th>
<th>PhD, MD/PhD or MD?</th>
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<tr>
<td>For Current Undergraduate Students and Mentors</td>
<td>For Current Graduate Students and Others</td>
<td>For Current Undergraduate Students and Mentors</td>
<td>For current Undergraduate Students</td>
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We invite visiting faculty mentors to join us for a conversation about what Emory looks for and we hope you will share your perceptions of the process. Members of several graduate admissions programs will be present.

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 you 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.

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**September 20 · 10:00 – 10:50 am**

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<th>The Emory PhD Experience: Succeeding in a Graduate Program</th>
<th>Life after Graduate School</th>
<th>Emory PhD Admissions Process (student session)</th>
<th>Developing a Career Plan and Individual Development Plans</th>
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<tr>
<td>For Undergraduate Students</td>
<td>For Current Graduate Students and Mentors</td>
<td>For Current and Prospective Graduate Students</td>
<td>For Undergraduate, Graduate Students and Mentors</td>
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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.

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. It will also have information from the Office of Postdoctoral Education.

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?

**myidp.sciencecareers.org**

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**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) [cse.emory.edu/home/projects/students/sure.html](http://cse.emory.edu/home/projects/students/sure.html)
- Pediatric Engineering Research Summer Experience (PERSE)
- Summer Undergraduate Program in Emory Renal Research (SUPERR)
- Center for Stereoselective C-H Functionalization (CCHF)
- REUs and NIH programs

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*Gillian Hue and Mitsi Blount, organizers*
*IMSD students organized by Pat Marsteller and Amanda James*
*Lou Ann Brown and Gaia Vasilver-Shamis, organizers*
*Damon Williams and members of Grad admissions committees*
*Pat Marsteller, organizer*
Body modifications have become commonplace in our society, whether they be mundane daily alterations (such as makeup use), more severe and invasive ones (rhinoplasty or breast augmentation), or those that might be artistic and permanent (tattoos and piercings). Some body modifications are widely accepted, while others are more stigmatized. Skin bleaching is a body modification that has become common in some developing countries. The present study examined how racial identity predicted perceptions of and attitudes toward various body modifications, with a special emphasis on skin bleaching. We were particularly interested in understanding whether these attitudes vary as a function of the circumstances in which the skin bleacher was found herself. In the present study, 41 African American women completed the Multidimensional Inventory for Black Identity, a measure of attitudes toward various body modifications, among other measures. We found that assimilation was the only dimension of the MIBI positively correlated with approval of skin bleaching. Participants were more likely to approve of skin bleaching if the skin bleacher was from a developing country trying to provide for her family. Women were less likely to approve body modifications that were permanent and have racial overtones. They were most disapproving of body modifications that were considered both permanent and racially motivated. The data suggest that, overall, women disapprove of skin bleaching; however, if someone has to work the system to change it, then it is relatively acceptable to skin bleach.

Eph receptor tyrosine kinases (EphRs) and their cognate ephrin ligands are cell surface molecules that have both attractive and repulsive guidance roles during development. Multiple EphRs and ephrins are expressed in vertebrates, and often exhibit promiscuous binding and overlapping expression. The nematode C. elegans is an ideal system to study EphR/ephrin function, as there are only four ephrin genes (efn-1 through efn-4) and one EphR (vab-1). We recently showed that efn-4 is necessary for primary neurite outgrowth in AIY-class interneurons. However, loss-of-function (l.o.f.) mutations in the vab-1 gene do not mirror efn-4 phenotypes, suggesting that a novel receptor may exist for efn-4. In addition, vab-1 mutants show distinct defects in AIY neuron ventral plexus formation. This region has multiple synapses, suggesting possible roles for vab-1 in shaping this key communication hub. A kinase-dead allele of vab-1 exhibits the same defect as the null mutant, suggesting that an ephrin-to-EphR forward signal is required for AIY plexus morphology. In addition, efn-1 l.o.f. mutants broadly recapitulate vab-1/EphR phenotypes, suggesting that it is the primary ephrin ligand required for this developmental event, although we are also using double and triple ephrin mutant combinations to determine whether the ephrins function in concert with each other. Finally, germ line microinjection of tissue-specific expression constructs will be used to confirm whether the EphR/ephrin pathway functions cell autonomously or not during ventral plexus formation.
The common skin and nail conditions “athlete’s foot” (tinea pedis), “ringworm” (tinea corporis) and onychomycosis result from infection by fungi known as dermatophytes. It can be challenging for clinicians to differentiate dermatophytic infections from other common dermatologic conditions by visual inspection alone. This can pose a problem for patients, as treatment for an inflammatory condition may worsen a fungal infection, and vice versa. To improve diagnostic accuracy, standard dermatologic practice involves the microscopic examination of skin scrapings (KOH prep) to visualize fungal structures. Prior work has shown that fluorescence microscopy using calcofluor white (CFW), an inexpensive staining agent that fluoresces when bound to the fungal cell wall, significantly improves the sensitivity and specificity of KOH prep to visualize fungal structures. A major barrier to adoption of this technique by clinicians is the lack of a fluorescent microscope in a typical dermatologic or primary care practice, due to the equipment’s large size, high cost, and technical complexity. The primary goal of this project was to design a compact, lightweight, low-cost, mobile phone-based fluorescence microscope to aid in the diagnosis of skin disease, and validate its use with clinical samples. Towards this end, we have designed and built a compact phone-based fluorescence microscope for under $50 that implements UV LED excitation with CFW staining. We demonstrate its use in successful detection of the most common dermatophyte, Trichophyton rubrum. Images obtained with our prototype are shown to be comparable to those obtained with a high end, commercially available fluorescence microscope.

Plasmodium falciparum causes malignant tertian malaria in West Africa, leading to about 630,000 deaths annually. Currently, there is no vaccine for this disease, but there are multiple candidates that include the use of surface antigens of P. falciparum. The purpose of this study was to determine the relationship between P. falciparum antigens and the amount of antibodies produced in individuals in the Central Region of Ghana. The two antigens studied were the schizont extract and glutamate-rich protein (GLURP). Samples were collected from individuals at the University of Cape Coast and donors from Assin Mensia. The samples were from people who were non-sick and without malaria in the past two months and the control group consisted of individuals who had reported malaria-like symptoms during that time. Blood smears were done to determine the parasitemia levels and plasma was extracted for enzyme-linked immunosorbent assay (ELISA). Samples were screened for other infections, specifically syphilis, hepatitis B and hepatitis C. Only 20% of the individuals who reported malaria-like symptoms actually had the parasite in their blood. Non-sick immune adults had higher antibody levels to both the schizont extract and GLURP. Populations without malaria infections, but other communicable infections also had higher antibodies to schizont extract and GLURP. Our results suggest that repeated exposure to the malaria parasite can produce stable immunity and other communicable infections may lower the antibody levels of individuals in malaria-endemic areas.

Recently, superhydrophobic surfaces have attracted attention due to potential practical applications such as self-cleaning, anti-icing, anti-bacterial and reduction of drag. Superhydrophobic surfaces are by definition surfaces with water contact angles (WCA) larger than 150 degrees and water sliding angle less than 10 degrees. Fabrication of superhydrophobic surfaces depends on the ability to control and modify the surface chemistry and surface roughness of the surface. Superhydrophobic surfaces are obtained when the surface exhibits low surface energy and appropriate surface roughness. In this project superhydrophobic surfaces were fabricated and tested to observe bacterial reduction compared to surfaces that are not superhydrophobic. Superhydrophobic surfaces were prepared by coating etched 6061 Al mirror like sheet of size 5 cm x 1.5 cm with 2 mm thickness (McMaster-Carr) with a composite nano-structure coating. The nano-structure coating was prepared with polyurethane (MINWAX) and by synthesizing cerium dioxide nanoparticles via hydrothermal method. A tetracycline (TC) suspension was prepared and 1 ml of the suspension was applied to superhydrophobic surfaces and control samples. These surfaces were allowed to dry and then stamped onto Tryptic Soy Agar and incubated for 24 hours. It was observed that superhydrophobic surfaces had resulted in fewer bacteria colonies. Fluorescent microscopy, SEM, and AFM measurements will be taken to further investigate the bacterial interactions between the superhydrophobic surface and bacteria.
biochemical evidence that TREX1 can reduce HIV-1 DNA overexpression. SupT1 cells show that these PICs contained nucleus suggesting that TREX1 does not disrupt nuclear import of TREX1 overexpression of HIV-1 decreases HIV-1 DNA integration. Furthermore, analysis of abortive integration products in the nested real-time PCR. Our results illustrate that the expression on PIC activity and proviral integration was acute. The human immunodeficiency virus type 1 (HIV-1) is known to escape the host immune system resulting in the development of acquired immunodeficiency syndrome (AIDS). Studies suggest that the cellular Three Prime Repair Exonuclease (TREX1) enables HIV-1 to evade the innate immune detection by preventing the accumulation of cytoplasmic viral DNA. However, the exact step of the HIV-1 life cycle at which TREX1 degrades the viral DNA is unknown. HIV-1 replication involves reverse transcription of the viral RNA genome into a double stranded viral DNA (dsDNA). Even though the dsDNA could serve as a substrate for TREX1, it has been proposed that the preintegration complex (PIC) protects the dsDNA. To understand the mechanism by which the PIC-associated dsDNA is protected from TREX1 exonuclease activity, we are studying the effects of TREX1 on the integration activity of HIV-1 PICs. In initial studies, the effects of TREX1 expression on PIC activity and proviral integration was investigated. Viral DNA integration was examined by quantitative nested real-time PCR. Our results illustrate that the overexpression of TREX1 decreases HIV-1 DNA integration. Furthermore, analysis of abortive integration products in the nucleus suggest that TREX1 does not disrupt nuclear import of HIV-1 PIC-associated dsDNA. Isolation of PICs from TREX1 stably overexpressing SupT1 cells show that these PICs contained reduced integration activity. In summary, these data provide first biochemical evidence that TREX1 can reduce HIV-1 DNA integration.
Mammalian target of rapamycin (mTOR) has been widely implicated as a critical sensor of nutrient sufficiency in dividing cells, and is commonly dysregulated in 70% of all cancers. Emerging evidence has suggested a significant role of phosphatidic acid (PA), a central metabolite in the synthesis of membrane phospholipids, in the stability and activity of the mTOR complex in dividing cells. This suggests that PA is critical for sensing the presence of sufficient lipids for membrane biosynthesis in proliferating cells. This study had three specific aims: 1) To study the effect of exogenous lipids on the mTOR complex, 2) examine the role LPAAT plays in oleic acid - induced mTOR activation, and 3) ascertain the significance of lipid-sensing by mTOR in mutant KRAS-driven cancer cells.

Emerging evidence suggests the significance of LPAAT in the regulation of mTOR. We showed compensatory production of PA under stressful conditions, where de novo PA production through LPAAT increases when alternative pathways are compromised. We have uncovered mTOR’s role in lipid sensing by proving the exogenous fatty acid, oleate, activates mTOR through PA generation. Furthermore, decreases in mTOR activity were evident with LPAAT knockdown after addition of exogenous fatty acids. Lastly, levels of the ACSL5 protein, located upstream of LPAAT in the same pathway, are present in significantly higher amounts in KRAS-driven cancer cells. These results suggest that de novo-generated PA is critical for sensing the presence of sufficient lipids, as well as driving mTOR to allow cell growth and proliferation.

Rigorous research has gone into the development of titanium-based anticancer drugs due to their broad spectrum of cytotoxic effects and lack of cross resistance with platinum-based compounds towards cancer cells. Unfortunately, hydrolytic instability followed by metal precipitation presumably has prevented these from advancing to clinical trials. Insoluble titanium compounds such as titanium dioxide (TiO2) have the potential of anticancer activity due to their capability of generating reactive oxygen species (ROS) when exposed to an energy source. Previous studies have shown that Human Serum Albumin binding of the former drug candidate titanocene dichloride prevents it from dissociating and the metal from precipitating as TiO2. Since cancer cells accumulate higher levels of HSA than normal cells for nutrition due to a higher metabolic requirement, by binding titanocene to HSA, the complex can be delivered intact to cancer cells. This interaction can have a major impact on the compound’s cytotoxicity. In the cellular environment we propose that the protein will undergo enzymatic digestion, exposing the titanium compound to aqueous surroundings thus promoting its precipitation as TiO2. Subsequent UV activation is expected to yield ROS. Differential Scanning Calorimetry suggests unaltered HSA stability when titanium bound, meanwhile, periodic colorimetric assays demonstrate that titanium concentration decreases in the presence of cell lysate proteases. Further analysis through Energy Dispersive Spectroscopy confirms the presence of titanium in the sample precipitate. Current analysis includes cell metal uptake measurements in addition to X-Ray Powder Diffraction in order to confirm the formation of TiO2 and the feasibility of ROS generation.
Amyloid fibrils are conformations of misfolded proteins with a stable Beta-sheet structure. They are believed to be the main cause of neurodegenerative disorders such as Alzheimer’s and Parkinson’s disease. We have shown that by adding sulfhydric acid (H2S) to hen egg white lysozyme (HEWL) amyloid fibers are inhibited (UPR-Mayaguez Patent). This inhibition results in small spherical aggregates of unsorted protein that exhibit almost no cytotoxicity. In the work presented here, the concentration of H2S in samples of HEWL was varied to explore the associated soft matter assembly and changes in protein conformation. These changes were followed by Th1 fluorescence to determine the behavior of the Beta-sheet structure. Samples without H2S yielded high concentrations of Beta-sheet conformations, consistent with amyloid aggregates. However, the samples in the presence of H2S show little to no Beta-sheet structures. This indicates that the newly formed structures have a vastly different configuration. In this study, various concentrations of CaCl2, ranging from 0-1.0M, are added to aqueous buffered solutions of both control and 295nm-irradiated a-crystallin and are monitored using fluorescence and UV-Visible spectroscopy to see the effect of calcium ions on the function of a-crystallin. UV-Visible absorbance spectroscopy will be used to monitor the absorbance at 295nm, which is specific to the tryptophan amino acid in a-crystallin. These results provide insights into the interaction of peptides with graphene on the functional groups of a-crystallin and graphene. The investigation on the interaction of small molecules with graphene can also provide insight into the binding behavior of larger biomolecules. This knowledge could facilitate the development of tailored peptide-functionalized graphene for sensitive biochemical sensors.

The protein a-crystallin, which is located in the ocular lens, plays a key role in maintaining lens transparency. Studies have shown that a-crystallin acts as a chaperone to protect damaged proteins, such as B-crystallin, from unfolding or aggregating under stressed conditions. Although the exact mechanism is unknown, there is some evidence that supports the idea that a-crystallin protects B-crystallin by allowing its hydrophobic areas to interact with the damaged proteins. Several factors, such as exposure to UV radiation and changes in ionic strength, may affect the chaperone-like behavior of a-crystallin by changing its configuration. In this study, various concentrations of CaCl2, ranging from 0-1.0M, are added to aqueous buffered solutions of both control and 295nm-irradiated a-crystallin and are monitored using fluorescence and UV-Visible spectroscopy to see the effect of calcium ions on the function of a-crystallin. UV-Visible absorbance spectroscopy will be used to monitor the absorbance at 295nm, which is specific to the tryptophan amino acid in a-crystallin. These results provide insights into the interaction of peptides with graphene on the functional groups of a-crystallin and graphene. The investigation on the interaction of small molecules with graphene can also provide insight into the binding behavior of larger biomolecules. This knowledge could facilitate the development of tailored peptide-functionalized graphene for sensitive biochemical sensors.

Graphene has attracted much interest in recent years due to its unique properties and characteristics. It is considered to be the strongest, flexible, conductive and most transparent material known. Noncovalent functionalization of graphene with peptides is a promising method for producing novel biochemical sensors with high sensitivity and selectivity. In this study, graphene was synthesized using Hummers/Olfeman method and peptides are then selected as possible binding candidates on graphene sheets. Both graphene and complexes were characterized with IR, NMR, and UV spectroscopy. In order to better understand the binding mode of peptides on the graphene surface, the amino acids E (Glutamic Acid), K (Lysine), L (Leucine), M (Methionine), P (Proline), and Q (Gluatamine) are modeled by Gauss View and Python and further simulated by VASP. The objective of this project is to understand the relationship between peptides and graphene host and locate possible binding parameters such as the distance and conformation. The investigation on the interaction of peptides with graphene can also provide insight into the binding behavior of larger biomolecules. This knowledge could facilitate the development of tailored peptide-functionalized graphene for sensitive biochemical sensors.

Computational simulations of protein ligand complexes are used to estimate the binding affinities of several potential ligands of the liver X receptor (LXR) and its two isoforms, especially for the liver X receptor (LXR) and its two isoforms, both with very similar binding pockets. A computational approach is an effective way to test potential isoform selective agonists for the liver X receptor (LXR) and its two isoforms, especially for designing pharmaceuticals for atherosclerosis, colon cancer, and other diseases. It has been observed that nonselective agonists lower serum cholesterol levels and also tend to raise triglyceride levels in the liver, which can lead to serious medical issues, while LXR selective agonists tend to lower cholesterol levels without affecting triglyceride levels; thus, there is a strong drive to develop selective liver X receptor (LXR) and its two isoforms, especially for designing pharmaceuticals for atherosclerosis, colon cancer, and other diseases. It has been observed that nonselective agonists lower serum cholesterol levels and also tend to raise triglyceride levels in the liver, which can lead to serious medical issues, while LXR selective agonists tend to lower cholesterol levels without affecting triglyceride levels; thus, there is a strong drive to develop selective liver X receptor (LXR) and its two isoforms, especially for designing pharmaceuticals for atherosclerosis, colon cancer, and other diseases. It has been observed that nonselective agonists lower serum cholesterol levels and also tend to raise triglyceride levels in the liver, which can lead to serious medical issues, while LXR selective agonists tend to lower cholesterol levels without affecting triglyceride levels; thus, there is a strong drive to develop selective liver X receptor (LXR) and its two isoforms.
Gout, a painful form of inflammatory arthritis, is a uric acid crystal deposition disease with limited treatment. It is caused by elevated levels of uric acid in the body due to the metabolism of dietary purines. As the disease progresses, uric acid crystals accumulate in synovial joints forming painful masses called tophi. Currently, treatments such as anti-inflammatory drugs (NSAIDS), colchicine, and systemic glucocorticoid have proven to stimulate unfavorable side-effects. An alternative method of treatment is therefore essential. In this study, we demonstrate a novel method of treating gout using the Metal-Assisted and Microwave-Accelerated Evaporative De-crystallization technique (MAMAD). This technique involves using microwave energy and gold nanoparticles, which behave as "nano-bullets", to rapidly disrupt the crystal lattice structures of biological crystals placed on 2D surfaces (i.e. Glass and Poly(methyl methacrylate) - PMMA). Furthermore, biological molecules of various sizes and compositions, small uric acid crystals, medium and large l-alanine crystals, were studied as models for gout and toph formation. Our results show that the MAMAD technique is effective at reducing the size and number of uric acid and l-alanine crystals of all sizes by >40% when heated intermittently for periods of 60 seconds and 120 seconds with low powered microwave.

Diabetes has evolved into a high priority global epidemic. The current treatment involves timely injection of insulin to maintain glucose homeostasis. However, alternate holistic treatments that directly target the repair of beta cells to stimulate endogenous insulin production are desperately needed. Erythropoietin (EPO) is a glycoprotein hormone produced by the kidneys that plays an invaluable role in blood cell production. Surprisingly, however, it has also been shown to protect heart, brain and pancreatic tissues from various injuries. Despite its exceptional tissue-protective activities in animal models, it has not found use in humans because of its side effects and production costs. Asialo-erythropoietin is a glycoprotein hormone produced by the kidneys that plays an invaluable role in blood cell production. Surprisingly, however, it has also been shown to protect heart, brain and pancreatic tissues from various injuries. Despite its exceptional tissue-protective activities in animal models, it has not found use in humans because of its side effects and production costs. Asialo-erythropoietin is a glycoprotein hormone produced by the kidneys that plays an invaluable role in blood cell production. Surprisingly, however, it has also been shown to protect heart, brain and pancreatic tissues from various injuries. Despite its exceptional tissue-protective activities in animal models, it has not found use in humans because of its side effects and production costs. Asialo-erythropoietin is a glycoprotein hormone produced by the kidneys that plays an invaluable role in blood cell production. Surprisingly, however, it has also been shown to protect heart, brain and pancreatic tissues from various injuries. Despite its exceptional tissue-protective activities in animal models, it has not found use in humans because of its side effects and production costs. Asialo-erythropoietin is a glycoprotein hormone produced by the kidneys that plays an invaluable role in blood cell production. Surprisingly, however, it has also been shown to protect heart, brain and pancreatic tissues from various injuries. Despite its exceptional tissue-protective activities in animal models, it has not found use in humans because of its side effects and production costs.
Amphibian fibrils are formed by soluble proteins that, through the process of protein unfolding, assemble into undegradable insoluble fibers. These amphibian fibrils are associated to many types of diseases, like Diabetes Type 2, that are characterized by the specific protein or peptide chain that aggregates extracellularly to a body tissue. The process of protein unfolding and fibrillation can be promoted by applying extreme conditions of high temperature and low pH to the desired protein. It has been proven that by adding a hydrogen sulfide (H2S), hen egg white lysozyme (HEWL) amphibian fibrils can be inhibited (UPR Patent). Similar experiments have been carried out using insulin from Bovine Pancreas (IBP). With the goal of thoroughly studying these advances, much awaits to be known about the structure and activity of catalases from fungal sources. Pichia pastoris is a yeast enzymes, have been structurally characterized by X-ray crystallography from organisms such as Penicillium vitale and Micrococcus lusodeiketics. More recently, the structure of Hansenula polymorpha catalase has been reported. Despite these advances, much awaits to be known about the structure and activity of catalases from fungal sources. Pichia pastoris is a model methlylophylic yeast in peroxisomal research and biotechnology with applications ranging from food to pharmaceutical industry. In order to fully understand the enzymatic activity and structure of the P. pastoris catalase (PcPcAT), we have cloned, overexpressed and purified it in order to crystallize PcPcAT and determine its three-dimensional structure by X-ray crystallography. Crystals of PcPcAT were diffracted in the ALBA synchontron light source. The best crystals diffracted to 2.3Å. Angstrom resolution and the complete structure determination is in progress. In conclusion, the enzymatic activity and structural results found will provide further biological knowledge about the PcPcAT as well as provide information for future industrial applications.
Vascular dysfunction is associated with obstructed blood flow, inflammation and vasoconstriction. Because type II diabetes (T2DM) is characterized by hyperglycemia and insulin resistance, how blood vessels transport insulin and glucose within the body is important. Hyperglycemia leads to vasoconstriction and inflammation. An increase in force pressing against the wall of blood vessels leads to the vessels stretching to regulate blood flow, therefore creating a greater demand of workload on the body. Moreover, blood flow is obstructed, as well as a lower bioavailability. Because NO and Hsp90 are essential for vasodilation and Hsp90 aids in protection against inflammation, diminished amounts instigate vascular dysfunction and enhanced risks of cardiovascular abnormalities. Both heat and exercise are known to improve the presence of hsp90 and NO. Thus, we utilized heat acclimation (acute heat and exercise) in an effort to treat vascular dysfunction in T2DM. Both diabetic Goto-Kakizaki (GK) and non-diabetic Wistar rodents (control) were treated daily with heat acclimation (HA) for 14 days. Our results indicate that the concentration of Hsp70 in GK rodents increased by 31% in comparison to the control, which normalizes to the value of the Wistar control, hsp90 concentrations are also augmented. Improvements in the diabetic NO concentrations (1.439 +/- 0.8525 uM) were also observed following HA treatment. Blood glucose levels declined, the blood pressure is diminished and insulin sensitivity is enhanced and blood glucose levels decline. Similarly, heat treatment also exhibits beneficial results that aid in the control of insulin. Thus, our aim was to utilize a combination of acute heat and exercise, known as heat acclimation, to regulate insulin resistance and weight gain in T2DM. Heat acclimation was used for both Goto Kakizaki (GK, type II diabetic) and Wistar (non-diabetic) rats for a 14 day period. Daily, the rodents were placed on a treadmill inside a heated chamber (~42 degrees Celsius), and body mass was measured. Blood samples were collected to measure both blood glucose levels and insulin concentrations. Our results indicate that the insulin concentrations increased by 45% in the GK rodent when treated with heat acclimation in comparison to its respective control. Moreover, body mass and blood glucose levels were regulated within the treatment group. Thus, we conclude that heat acclimation positively impacts T2DM by controlling the key detrimental components of the disease.

Type II diabetes (T2DM) is a common disease that is marked by insulin resistance, hyperglycemia and obesity. During insulin resistance, precise regulation is put on the pancreatic beta cells in order to secrete abnormal amounts of insulin and to properly regulate blood glucose levels. Studies show that regular physical activity causes the body to become more sensitive to insulin and minimizes excessive weight gain. Consequently, insulin sensitivity is enhanced and blood glucose levels decline. Similarly, heat treatment also exhibits beneficial results that aid in the control of insulin. Thus, our aim was to utilize a combination of acute heat and exercise, known as heat acclimation, to regulate insulin resistance and weight gain in T2DM. Heat acclimation was used for both Goto Kakizaki (GK, type II diabetic) and Wistar (non-diabetic) rats for a 14 day period. Daily, the rodents were placed on a treadmill inside a heated chamber (~42 degrees Celsius), and body mass was measured. Blood samples were collected to measure both blood glucose levels and insulin concentrations. Our results indicate that the insulin concentrations increased by 45% in the GK rodent when treated with heat acclimation in comparison to its respective control. Moreover, body mass and blood glucose levels were regulated within the treatment group. Thus, we conclude that heat acclimation positively impacts T2DM by controlling the key detrimental components of the disease.

Increased epigenetic and transcriptome regulation of conventional human pluripotent stem cells populations cause a limited differentiation capacity in vitro. In contrast, the murine embryonic stem cell (mESC) is the most naive in vitro pluripotent state proven by hypo-methylation and an ability to form chimeras. Our lab has produced a new class of human stem cells in stable naive pluripotent ground state using an optimized WNT-MEK/ERK inhibition strategy called LIF-3i. LIF-3i-reverted hPSCs distinguish themselves by their ability to undergo single-cell, clonogenic enzymatic passage and robust proliferation into uniform, mESC-like dome-shaped colonies. qRT-PCR and immunofluorescence studies revealed higher expressions naive markers (e.g., NANOG, STEM, NR5A2 and E-CADHERIN), and loss of XIST expression compared to conventional hPSC. Currently, further primitive characterizations are being analyzed via homologous recombination and telomere length assays. Our LIF-3i-hPSCs have also shown significant increase in hematopoietic differentiation potential and greater expression of CD34+ and KDR+ progenitors, as well as greater self-renewal capacity. To test the engraftment potential of these cells, vascular and hematopoietic progenitors will be inserted into chicken embryos and engraftment will be analyzed 14 days after incubation. Additionally, to further characterize the differentiation of hematopoietic progenitors derived from nHPS, single-cell qPCR will be completed. With current and on-going experiments, we have concluded that the pluripotent capacity of the starting population plays a significant role in differentiation potency. Additionally, we show that our LIF-3i system is able to produce a stable naive pluripotent state that is epigenetically and transcriptionally comparable to that of mESCs.

Mesenchymal Stem Cell (MSC)-based therapies developed for clinical purposes rely on the use of fetal bovine serum (FBS) for the ex vivo expansion of MSCs. FBS constitutes a xenogenic media supplement and has the potential to alter MSC phenotype and render the cells immunogenic. Replacing FBS with a media homologous to the species of interest would likely decrease immune-mediated host reactions. Platelet lysate (PL) has been used for human MSC expansion. However, there is little data available to determine whether PL may trigger inflammatory responses when exposed to reactive white blood cells such as monocytes. We test the hypothesis that equine PL (ePL) suppresses the production of TNF-a from Lipopolysaccharide (LPS)-stimulated equine monocytes. We test the hypothesis that equine PL (ePL) suppresses the production of TNF-a from Lipopolysaccharide (LPS)-stimulated equine monocytes. Equine platelet concentrate was obtained via platelet apheresis from 6 equine blood donors and ePL generated. Equine monocytes were incubated in presence of donor horse serum (DHS), FBS, individual horse donor ePL or pooled ePL. Equine monocytes were incubated with E. coli LPS and/or DHS and/or pooled ePL in various concentrations. Cell culture supernatants were assayed for the production of TNF-a. Pooled equine PL significantly reduced TNF-a production from LPS-stimulated equine monocytes compared to those incubated with DHS or FBS. Moreover, ePL was able to significantly reduce TNF-a production from equine monocytes even when monocytes were co-incubated with DHS and ePL. Our data suggests that ePL is able to suppress the release of inflammatory cytokines following incubation with stimulated and unstimulated equine monocytes. The mechanism behind the ePL-mediated monocyte suppressing activity is subject to continued investigation.
The neural development gene, kal-1, regulates neurite branching and cell adhesion. Humans bearing kal-1 mutations develop X-linked Kallmann syndrome (KS) and have defects in olfactory nerve development, leading to a lack of smell, with secondary defects in gonadotropin release and failure to undergo spontaneous puberty. This gene is conserved in C. elegans, to the point where it has been demonstrated that the human kal-1 (ZNF804B) can rescue kal-1 loss of function mutants. Over 20 loci have been associated with KS to date, although 65% of KS patients have no obvious lesions in these genes, suggesting that additional KS loci remain undiscovered. We hypothesize that transcription factors required for the control of KS genes may represent novel KS loci. Bioinformatic approaches predict that multiple transcription factors can bind to the kal-1 regulatory region including cnd-1, the C. elegans ortholog of NeuroD. cnd-1 (ju23) mutant worms disrupt embryonic kal-1 (GFP) reporter expression. We are taking a transcription approach to better understand the gene regulatory network between cnd-1 and kal-1. Transcriptomes of wild type and cnd-1 (ju23) mutant embryos, in conjunction with modENCODE and interactome data, will be used to find potential genes involved in this network. Candidate regulatory genes will be validated by electrophoretic mobility shift assays to determine in vitro binding specificity. These will be supported by in vivo genetic studies that examine how TF loss-of-function mutations affect kal-1-GFP expression. Congenital heart disease (CHD), encompassing any abnormality within the heart's anatomical structure present at birth, is the most common type of birth defect with 1.35 million babies born with lethal CHD each year. Ventricular defects account for 33% of CHD cases, occurring when the interventricular septum (IVS) does not fully develop. The septum appears to arise from the interaction between two populations of cells, one from the first heart field and another from the second heart field. However, despite the severe clinical impacts of septal defects, the cellular and molecular events governing the integration and contribution of these two populations of cells to the IVS have yet to be established. To elucidate mechanisms of septation, we used a reporter mouse that allows lineage tracing of individual clones across the period of heart development. Our results show that cells within the second heart field comprise cells within the IVS. To begin to explore the mechanisms by which these cells integrate and contribute to the IVS, we used mice that are null for the transcription factor Casz1, a gene known to be essential for mammalian IVS formation. By repeating cell fate mapping, we went on to show that there was a marked reduction in the number of secondary heart field derived clones in the IVS of Casz1 mice compared to wildtype mice. Taken together, these studies have established a role for the second heart field in IVS formation and have determined the cellular requirements for Casz1 in these processes.

Prostate cancer is the most diagnosed cancer and the second leading cause of death in men in the United States. Epithelial-mesenchymal transition (EMT) plays a critical role in cancer progression and metastasis by decreasing epithelial-associated gene expression (such as E-cadherin) and increasing mesenchymal gene expression (such as vimentin). Reactive Oxygen Species (ROS) and High mobility group a2 (HMGA2) have been shown to promote EMT in separate studies. Interestingly, wild-type HMGA2 and truncated (lacking the 3’ UTR) are overexpressed in many cancers. Additionally, we have reported that camalexin, a 3-thiazol-2-yl-indole, may target aggressive prostate cancer cells by ROS-mediated apoptosis. To date, no link has been reported between ROS and HMGA2. We hypothesized that HMGA2 can regulate EMT in prostate cancer cell lines via ROS, and that camalexin may antagonize HMGA2 signaling. Baseline analysis of HMGA2 showed high expression in PCa3 and ARCaP, which are considered to be aggressive cells, compared to normal epithelial cells. Stable overexpression of HMGA2 (wild-type and truncated) in LNCaP cells increased ROS particularly in LNCaP cells compared to wildtype LNCaP. Taken together, these studies have established a role for the second heart field in IVS formation and have determined the cellular requirements for Casz1 in these processes.
Several psychiatric disorders are characterized by deficits in the social domain, and variation in the oxytocin receptor gene (Oxtr) may contribute to diversity in social cognition and behavior. Voles provide a unique opportunity to explore how Oxtr variation influences brain and behavioral phenotypes. Among prairie voles, there is extraordinary individual variation in Oxtr density in the striatum that predicts diversity in allo-parental behavior and resilience to early-life social isolation. A linkage block of 14 polymorphisms in the prairie vole Oxtr predicts >80% of variation in striatal receptor density, but not other brain areas. By aligning this linkage block to the mouse ENCODE data from whole brain, one SNP, NT123379, was identified to be in a region marked with features of transcriptional regulation. Here, we assessed CTCF interactions with NT123379 and a distal SNP that did not align with markers of transcriptional regulation in prairie vole striatum and cortex using Chromatin Immunoprecipitation and quantitative Polymerase Chain Reaction (ChiP-qPCR). We confirm a significant 4-fold enrichment for CTCF binding in vole striatum and cortex (n=6) at NT123379, consistent with the possibility that this SNP directly influences striatal variation. Future directions will be to further define regulatory factor interactions across the vole Oxtr in tissue from several brain regions using ChiP-seq, and to assess allelic differences. This will provide molecular genetic evidence for the mechanism underlying how Oxtr variation may influence social behavior as well as psychopathology.

Maternal response to infants requires sensitivity and attention to infant-specific social cues, such as infant vocalizations. Shortly after the influx of hormones associated with parturition, mother mice rapidly begin responding to behaviorally relevant pup isolation calls. Non-mothers can reach the same level of maternal responsiveness to these cues after sufficient pup experience, a process that can be enhanced in the presence of the hormone estrogen. The ability for pup vocalizations to elicit maternal responses depends on the auditory cortex (AC), where neural plasticity in the encoding of pup calls is thought to enhance their salience. The underlying molecular mechanisms enacted by estrogen and social pup experience to enhance AC processing are currently unknown. Of particular interest is the neuregululator Norepinephrine (NE), whose main cortical source derives from activity in the locus coeruleus (LC). A functioning NE system is necessary for normal maternal behavioral responses to infant cues. Moreover, both the LC and AC express estrogen receptors, providing a potential substrate in both brain areas for estrogen's effects on experience-dependent changes in the responsiveness to pup calls. We therefore tested the effects of estrogen's exposure and pup care experience using a 2x2 design in virgin female mice. Mice were given either 17-beta estradiol (E2) or vehicle implants, and cohooused either with a dam and litter (co-carer, CC) or with adult female littermaters. We examined the response to playback of pup calls in the LC, primary AC, and secondary AC using the expression of the immediate early gene c-fos (c-fos-ir) as a measure of neural activity. The c-fos-ir in the primary AC, the site of initial cortical sound processing, was highly correlated (r = 0.91) with that of the secondary AC, a higher order associative sound processing area. In both the primary and secondary AC we observed a main effect of pup experience (primary: F (1,10) = 7.7044, p = 0.034; and secondary: F (1,10) = 11.0448, p = 0.033), which reduced call-evoked c-fos-ir in the LC, we found an interaction between estrogen and pup experience in response to pup call playback (F (1,29) = 8.308, p = 0.007). Interestingly, while the primary AC's activity was not correlated with that of the LC (r = 0.06), the secondary AC and LC were negatively correlated (r = -0.47) suggesting an association between higher order auditory processing and neural activity. While the pattern of LC response across animal groups could not be simply explained by the pattern of AC activation, it was notable that E2-CC mice showed a particularly large pup call response in the LC, c-fos-ir, despite having the lowest relative AC response (i.e., greatest plasticity). These results support the hypothesis that the specific conjunction of pup experience under the influence of estrogen heights the NE system's response to pup calls, enabling greater plasticity in AC and making those vocalizations more salient.

Background: Childhood maltreatment is associated with increased risk for psychopathology, and social and cognitive deficits. This is likely due to alterations in cortico-limbic circuits (i.e. prefrontal cortex (PFC) and amygdala connectivity) critical for emotional and stress regulation, which are sensitive to early experience and stress due to their protracted development. Methods: This study used a well-established rhesus monkey model of maltreatment (MALT), which consists of spontaneous and comorbid physical abuse and rejection, leading to infant distress. Structural and resting state fMRI scans were collected at postnatal ages 2 weeks, 3, 6, 12, 18 months, and adolescence in 13 animals with history of infant maltreatment (7 males, 6 females) and 13 controls (6 males, 7 females). Results: Resting state fMRI findings suggest reduced Amygdala-PFC functional connectivity (FC) in MALT animals, and an accelerated switch to negative coupling throughout development, especially between amygdala and mPFC and dIPFC, in comparison to controls. MALT animals also required longer training to discriminate safety signals during the AX+ /IBX- task, and had slowed RT when threat expressions were congruent with the cue, especially among females. Conclusions: These findings suggest developmental alterations in FC between amygdala and PFC regions (i.e. reduced FC) in MALT subjects, which could underlie their deficits in safety-signal learning and biased attention away from threat during adolescence.
While past research has shown human’s propensity to perceive others as evaluators, the ontogeny of this construct is underspecified. The current investigators explored the emergence of an evaluative audience perception (i.e., emerging sensitivity to others evaluation of the self) in infancy by capturing the first signs of behavior modification in the presence of an observer. Based on previous work on the development of self-consciousness emotions toward the end of the second year, 14–24 month old infants (N=49) were tested in a within-subjects novel task where the attention of an audience was manipulated to directly measure when children begin to behave differently when being observed. Results indicated that children begin to modify their behavior by 24 months, inhibiting their own desire to explore a novel toy in an ambiguous situation only when the experimenter was attentive. Study two (N=31) built upon study 1 to explore a novel toy in an ambiguous situation only when the experimenter was attentive, and the ontogeny of this construct is underspecified. The current investigation explored the emergence of an evaluative audience perception (i.e., emerging sensitivity to others evaluation of the self) in infancy by capturing the first signs of behavior modification in the presence of an observer. Based on previous work on the development of self-consciousness emotions toward the end of the second year, 14–24 month old infants (N=49) were tested in a within-subjects novel task where the attention of an audience was manipulated to directly measure when children begin to behave differently when being observed. Results indicated that children begin to modify their behavior by 24 months, inhibiting their own desire to explore a novel toy in an ambiguous situation only when the experimenter was attentive. Study two (N=31) built upon study 1 to explore a novel toy in an ambiguous situation only when the experimenter was attentive. Study two (N=31) built upon study 1 to explore a novel toy in an ambiguous situation only when the experimenter was attentive.

Cardiac vagal tone indexes infants’ physiological regulation and is reflected in the amplitude of respiratory sinus arrhythmia (RSA) (Porges et al., 2010). Greater stability of resting RSA has been related to indices of better autonomic state regulation (Bomstein & Suess 2000; Porges, 2009). Thus, it is important to better understand the correlates or predictors of resting RSA stability in infancy. Length of breastfeeding is one promising consideration in such a model. Breastfeeding’s benefits in relation to RSA may include: (1) breastmilk’s essential bioactive factors that contribute to optimal infant growth and development (Ballard & Morrow, 2013), and (2) the skin-to-skin contact between mother and infant. In support of these points, breastfed infants exhibited greater vagal stability than formula-fed infants (Pivik et al., 2015) and the somatosensory stimulation through skin-to-skin contact (kangaroo care) during the early postnatal period was found to promote vagal tone development (Field & Diego, 2008). Moreover, infants of prenatally depressed mothers have been found to have lower resting vagal tone (Field et al., 2006). We extended this line of research to study the role of duration of breastfeeding in associations between perinatal depression and infants’ resting RSA stability. We hypothesized that: (1) longer duration of breastfeeding (at least the American Academy of Pediatrics’ recommended 6 months) would be associated with more stable resting RSA over the course of infancy; (2) breastfeeding duration would significantly contribute to predicting resting RSA at 3, 6, and 12 months beyond the effects of maternal perinatal depression.

Social processing is supported by interconnected regions such as the limbic, temporal, and frontal lobes (Leopold, 2010). Within the frontal lobe, damage to the orbitofrontal cortex (OFC) may result in impaired emotional processing and inappropriate social behavior (Tsuchida & Fellows, 2012). OFC subregions may be differentially involved in primate social processing, however, damage in human studies is rarely confined to one subregion. Thus, we prepared adult macaques with lesions to OFC subregions, including BA12 (n=4), BA11/13 (n=5), BA14/25 (n=4), as well as controls (n=4). Subjects viewed 10-second social and nonsocial movies containing emotional or neutral content. Gaze was tracked using infrared eye-tracking. Regions of interest (ROIs) were hand-drawn on selected regions. Percent looking was calculated for each ROI out of total looking time. A RM-ANOVA was performed for each ROI with valence as the within measure and lesion as the between measure. Damage to BA12 and BA11/13 decreased looking to the eyes of social stimuli compared to controls and BA14 (F3,13=6.08, p< 0.01), yet had no effect on other regions. For negative stimuli, subjects looked more at the mouth and less at eyes and main figure (Mouth: F1,5,19=3.97, p=0.05; Eyes: F2,26=13.78, p< 0.01; Main Figure: F1,9,24.5=5.55, p=0.01) compared to more positively valenced stimuli. No interactions reached significance. To date, rodent models have been the most widely used models for exploring the effects of environmental factors on spermatogenesis. However, rodent spermatogenesis is distinctly different from human spermatogenesis and does not always recapitulate human exposure phenotypes. Alternatively, human embryonic stem cells can be differentiated into advanced spermatogenic lineages including spermatogonial stem cells and spermatogonia, primary spermatocytes, secondary spermatocytes, and spermatids and represent a more tractable model to investigate the effects of environmental exposures on human spermatogenesis. Using this innovative model, we have evaluated the acute effects of the flame retardants TDCPP, TBBP, HB10C, and TBBPA as male reproductive toxicants using hESCs as they proliferate during mitosis, progress through meiosis, and differentiate into haploid spermatids. Our approach identifies these flame retardants as reproductive toxicants and gives clues to their mechanisms of action and windows of susceptibility that lead to altered human spermatogenesis.
### Poster Presentations

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Chemistry, Physics, Math and Computer Science

Rotational Spectroscopy of Weakly-bound Molecules in Astrochemistry

Luyao Zou, Brian M. Hays, Susanna L. Widicus Weaver

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Reaction intermediates that are unstable under terrestrial conditions have been long postulated to be responsible to the complexity of interstellar chemistry in the star and planet formation. The lack of their astronomical detection is due to both the low abundance of these species and the lack of laboratory measurement of their rotational transitions, which are the fingerprints for the identification of interstellar molecules. In this poster, we present our design of a new laboratory millimeter-submillimeter spectrometer and detection technique for the search of spectral lines from these weakly bound clusters. The spectrometer design and the spectra of trans-HO$_3$ and Ar-H$_2$O cluster are presented.

Chemistry, Physics, Math and Computer Science

Binding, Folding, and Insertion of a β-hairpin Peptide at a Lipid Bilayer Surface: Molecular Dynamics Simulations

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Antimicrobial peptides (AMPs) are common in many biological systems and act as host defenses against microbial pathogens. Existing theories on how AMPs permeabilize lipid membranes still lack mechanistic detail. In this study, we investigate the interactions of SVS-1 (KVKVKVKVPPPTKVKVKVK), an anti-cancer β-hairpin peptide, with lipid bilayers using atomistic molecular dynamics (MD) simulations. In agreement with experiment, peptides in simulation bind strongly to anionic but not neutral bilayers. Unfolded peptides at the anionic surface were observed to undergo several folding and mis-folding pathways. Folded peptides at the surface did not spontaneously insert their hydrophobic faces into the bilayer on the 1 µs timescale, but kept their Lys-rich face downward toward the lipid headgroups. Upon the application of sufficient surface tension, the peptides were observed to “flip and dip” into the bilayer within ~100 ns. It is possible that the tension induced in a bilayer from the crowding effect of many peptides binding could be a significant influence on the insertion rate.

Chemistry, Physics, Math and Computer Science

Influence of Ultrahigh Molecular Weight on the Physical Aging of Thin Polystyrene Films

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Physical aging and the glass transition are intimately related, with the physical aging rate providing a measure of the stability of the glassy state formed. Previously, we have investigated the physical aging rate in thin supported polystyrene (PS) films finding that the local aging rate is correlated with the local glass transition temperature [Pye et al., Macromolecules 43, 8296 (2010)]. These studies were able to provide a measure of the depth to which bulk glassy dynamics are perturbed by the free surface interface, a distance much further than similar measures of liquid-like dynamics. Here, we present physical aging measurements of thin PS films using ellipsometry. Surprisingly, we observe a distinctive molecular weight dependence to the physical aging behavior of thin (30 nm thick) films not present in bulk (1000 nm thick) films for very high molecular weights (Mw > 3000 kg/mol). These results indicate that chain connectivity plays a subtle, but important role in how gradients of glassy dynamics are propagated between the free surface and substrate interfaces.

Chemistry, Physics, Math and Computer Science

Contribution of Quantum Fluctuations to Magnetoresistance

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The ability to control the static and dynamical states of nanomagnetic systems by spin currents has been crucial for the recent development of fast electronically controlled spintronic and magnonic nanodevices. These effects have been interpreted exclusively in terms of the interaction of spin current with the classical dynamical states of magnetization, as described by the spin transfer torque (STT) model. Here, we demonstrate STT effect that arises from the interaction of spin current with the quantum fluctuations of magnetization. In contrast to the classical STT, the quantum STT results in a singular dependence of magnetization fluctuations on current, providing a litmus test for this effect. Both our analysis and experimental measurements show that the quantum STT becomes dominant at temperatures below 10 Kelvin in common 3d ferromagnets such as Permalloy, and its contribution increases with increasing magnetic field. Our findings provide a conceptually new framework for the development of advanced nanomagnetic devices, with particularly significant implications for devices based on antiferromagnets where quantum STT is expected to dominate even at room temperature.
The acoustics of vocal production in songbirds is tightly regulated during both development and adulthood as birds progressively refine their song using sensory feedback to match an acoustic target. Here, we perturb this sensory feedback using headphones to shift the pitch (fundamental frequency) of song. When the pitch is shifted upwards (downwards), birds eventually learn to compensate and sing lower (higher), bringing the experienced pitch closer to the target. Paradoxically, the speed and amplitude of this motor learning decrease with increases in the introduced error size, so that birds respond rapidly to a small sensory perturbation, while seemingly never correcting a much bigger one. Similar results are observed broadly across the animal kingdom, and they do not derive from a limited plasticity of the adult brain since birds can compensate for a large error as long as the error is imposed gradually. We develop a mathematical model based on nonlinear Bayesian integration of two sensory modalities (one perturbed and the other not) that quantitatively explains all of these observations. The model makes predictions about the structure of the probability distribution of the pitches sung by birds during the pitch shift experiments, which we confirm using experimental data.

Speckle interferometry is a common method used to obtain astronomical images using ground-based telescopes to image through a turbulent atmosphere-telescope system. However, when imaging more complicated astronomical objects such as satellites, speckle interferometry methods necessitate the separate recovery of the object’s Fourier phase to obtain more detailed images. Bispectral methods are one approach to solving this complementary problem of phase recovery in speckle interferometry. They retrieve an object’s Fourier phase by matching it to the object’s bispectrum, a collectable statistical quantity from the speckle data. Mathematically, phase retrieval from the bispectrum can be formulated as a large-scale, non-linear inverse problem. We consider several optimization schemes from the literature for solving this phase retrieval problem. In particular, we focus on accelerating the speed and convergence of this optimization while maximizing the quality of the recovered image through efficient implementation, Hessian based optimization, and appropriate regularization.

Toxoplasma gondii is a zoonotic apicomplexan parasite with a broad host range among warm-blooded animals, with a global distribution. The parasite is the cause of toxoplasmosis, a significant health risk to pregnant women and the immunocompromised. Until recently, T. gondii was believed to exhibit an almost exclusively clonal population structure, consisting of few sexual recombination events. However, the Toxoplasma research community analyzed recently suggested that the population structure involves more sexual recombination than previously thought. Since the parasite can only undergo sexual recombination in the feline gut, it is difficult to know how frequently strains of T. gondii meet to facilitate sexual recombination. Understanding sex at the population level can be informative of how rapidly markers of pathogenesis may be moving throughout the population.

To quantify these events, we use two approaches, (i) an in silico population simulation, and (ii) a matrix clustering analysis using Matlab. For the in silico population simulation, we generate multiple hypothetical sub-populations in the form of simulated genome sequences using software for forward-genetics simulation. At different rates of sexual recombination, we generate new progeny populations. These in silico progeny are then compared to the measured natural Toxoplasma population to infer the rate of sexual recombination occurring in the natural population. The matrix clustering analysis will allow us to distinguish between individuals that are the result of sexual events, and those that are the result of clonal expansion (both sexual [inbreeding], and asexual). This comparison will allow us to construct proposed groups of sexually produced progeny.

Studies have shown Dengue Virus (DENV) presence in neotropical wildlife including bats, suggesting that bats may be susceptible to DENV infection. We aim to elucidate the role of house-roosting bats in DENV transmission. Households were sampled from high and low dengue incidence regions during rainy and dry seasons in Costa Rica. We captured 318 bats from 12 species in 29 households. Necropsies were performed in 205 bats to analyze virus presence in heart, lung, spleen, liver, intestine, kidney, and brain tissue. Histopathology studies from all organs showed no manifestation of disease or infection. Sera were analyzed by PRNT190 for a seroprevalence of 22% (53/241), and by PCR for 8.8% (28/318) positive bats for DENV RNA. From these 28 bats, 2 intestines were DENV RNA positive for the same dengue serotype detected in blood. Viral isolation from all positive organs or blood was unsuccessful. Viral load analysis in positive blood samples by qRT-PCR showed virus concentrations under the minimal dose required for mosquito infection.

Simultaneously, 651 mosquitoes were collected and analyzed for DENV and feeding preferences (bat cytochrome b). Three mosquitoes were found DENV positive and none was positive for bat cytochrome b. Our results suggest an accidental presence of DENV in bats probably caused from oral ingestion of infected mosquitoes. Phylogenetic analyses suggest also a spillover event from humans to bats. We conclude that bats in these urban environments do not sustain DENV amplification; not having a role as reservoirs, but function as an epidemiological dead-end host for DENV.
Invasive breast cancer is the second leading cause of cancer death among women in the United States with more than 230,000 expected cases annually. Progression of disease is associated with development of resistance to chemotherapy, allowing re-growth of the tumor and metastatic spread of cancer cells. Using a high-throughput assay we screened approximately 2000 approved and experimental therapeutic agents to test their potency when combined with blockade of CD47. The group with the most synergism belonged to drugs aimed at the mammalian target of rapamycin (mTOR) and the PI3K pathway. Elevated mTOR or a primary factor of therapeutic resistance in many cancers including breast cancer. Using the mTOR inhibitor rapamycin we tested whether combination with CD47 blockade would synergize to reduce breast cancer growth. We observed that targeting CD47 using an antisense morpholinor or humanized antibody potentiated the effect or rapamycin in MCF-7 cells. Moreover using a MCF-7 parental cell line resistant to rapamycin we observed that combination with anti-CD47 treatment sensitized cells to therapeutic treatment. The potenation of the antigrowth effect of rapamycin was also observed in the triple-negative breast cancer cell line MDA-MB-231 indicating that this effect may be independent of the estrogen receptor status. Moreover, targeting CD47 reduced glucose uptake suggesting that it may reduce glucose metabolism to sensitize cells to rapamycin therapy. Therefore targeting CD47 may inhibit cell bioenergetics to inhibit pro-tumorigenic pathways and restore sensitivity to anti-mTOR targeting drugs, which may lead to novel therapeutic combinations to improve the clinical outcomes of breast cancer patients.

Colorectal cancer (CRC) is the third most common diagnosed cancer and the third leading cause of cancer related deaths. It has been reported that colon cancer incidence and mortality rates are higher in men than woman, but there is yet a determined mechanistic link to show the factors that underlie the gender specific differences in CRC initiation and progression. Benzo(a)pyrene (B(a)P), a member of the polycyclic aromatic hydrocarbon (PAH) family of compounds is a well-characterized environmental toxicant proven to be a major contributor to the development of sporadic colon cancer. B(a)P, a ligand for the Aryl Hydrocarbon Receptor (AhR), could potentially have the capacity to bind to the Estrogen Receptor (ER) and interfere with ER signaling in female rats. This study aims to elucidate the protective effects of estrogen on B(a)P-induced colon cancer in adult female Polyposis In the Rat Colon (PIRC) model. Groups of female PIRC rats (n = 8) received 25, 50 and 100 ug B(a)P/kg body wt. via oral gavage for 60 days. Female rats that received no [B(a)P] treatment and males with corresponding doses of [B(a)P] served as controls. Female PIRC rats that received 25, 50 and 100 ug B(a)P/kg body wt. showed significant decrease in total polyp count when compared to males with respective doses. Polyp sizes of female PIRC rats receiving 25, 50 and 100 ug B(a)P/kg body wt. were also significant decreased when compared to males respectively. This research will provide insight into if and how estrogen protects females from colon cancer.

Hsp70 is highly conserved group of protein expressed in almost all mammalian cells. Normally, it acts as molecular chaperone by assisting proper folding-refolding of a newly formed peptide chain. Resveratrol (3, 4, 5 trihydroxystilbene) is a naturally occurring phytoalexin produced by some spermatophytes, such as grapevines, in response to injury. Resveratrol is an antioxidant, anti-inflammatory, anti-proliferative, proapoptotic, and antiangiogenic compound. The objective of this study was to elucidate the role of Resveratrol and its effect in modulating the expression of hsp70 in murine prostate cancer cells. To test this objective, prostate cancer (PCA) cells were cultured in DMEM/RPMI supplemented with 10% fetal bovine serum (FBS), penicillin 100 U/ml, streptomycin 100 ug/ml, 0.005mg/ml bovine insulin, and 10nm Dehydroepiandrosterone in 5% CO2 at 37°C. PCA cells were harvested by trypsinization after 4-5 day treatment and immunofluorescent analyses revealed that Snail, Cat L and CDP/CUX cleavage product expression in MCF-7 Snail cells and immunofluorescent and cell fractionation analyses. We observed more Snail, Cat L and CDP/CUX cleavage product expression in MCF-7 Snail cells as compared to MCF-7 control cells. Interestingly, immunofluorescent and cell fractionation analyses revealed that Snail expression promoted nuclear localization of Cat L which may promote EMT and metastasis.


cancer cell lines to evaluate the expression of Snail, Cat L, CDP/CUX and EMT marker expression by western blot and immunofluorescent analyses. We observed more Snail, Cat L and CDP/CUX cleavage product expression in MCF-7 Snail cells and TNBC cells as compared to MCF-7 control cells. Interestingly, immunofluorescent and cell fractionation analyses revealed that Snail overexpression promoted nuclear Cat L and CDP/CUX p110 isoform expression, and EMT which could be abrogated by Z-FY-CHO or MSKE. In conclusion, our study shows that Snail promotes nuclear localization of Cat L which may promote EMT via CDP/CUX, and that inhibition with MSKE may be a good therapeutic target for TNBC.
It has been shown that GnT-V induces abnormal beta 1,6 branches on PTPRT, which inhibits its phosphatase activity on STAT3. However, it hasn't been shown whether or not STAT3 induces the overexpression of GnT-V, and it is unknown whether IL-6 regulates glycan structure of secreted glycoproteins. Our hypothesis is that STAT3, once activated by IL-6, induces the overexpression of GnT-V, which will induce abnormal beta 1,6 branches on secreted glycoproteins, potentially facilitating cancer development. We used a new gas chromatography-mass spectrometry (GC-MS) based technique to quantify unique glycan features from glycoproteins secreted by HepG2 cells treated with IL-6. It was found that IL-6 induces beta 1,4 branching, beta 1,6 branching, fucosylation, and the presence of terminal galactose residues within glycoproteins secreted by HepG2 cells. These features are imparted to glycans by several known glycosyltransferases, including GnT-V, etc. The IL-6 mediated pathway, RAS and PI3K, are not active in HepG2 cells, the STAT3 pathway is the only mediated pathway that is suggested to be intact in HepG2 cells. Therefore, this suggests that the expression of the glycosyltransferase genes or glycosylases in question, are more likely being regulated by STAT3. Constant STAT3 activation has been reported in hepatocellular carcinoma, as well as GnT-V overexpression. Our results suggest a positive feedback loop in which STAT3 induces the overexpression of glycoproteins, such as GnT-V, that, through construction of abnormal glycan features, facilitates STAT3 activation, translocation to the nucleus, and further increased expression of glycoproteins.

The production of reactive oxygen species has been implicated in neurodegenerative disorders such as Parkinson's disease and Alzheimer's disease. In PD, monoamines such as dopamine are severely depleted. We have previously demonstrated in vivo, that monoamines are depleted in the brain prior to the degeneration of dopamine neurons induced by the Parkinson's inducing agent MPTP. The current study examined the effects of monoamines such as dopamine, noradrenaline, and serotonin on the activities of antioxidant enzymes in response to oxidative stress mediated by hydrogen peroxide and/or the Parkinson's inducing agent MPTP/MPP+. Studies were performed in primary neurons and cell cultures. Our objectives are to determine if: Monoamines prevent or exacerbate the production of ROS 2); determined if monoamines increase or decrease the activity of antioxidant enzymes, and 3); determine if monoamines prevent or exacerbate the loss of dopamine neurons. The results demonstrate that H2O2 significantly increased DCF labeling (a marker for ROS production) after 24 hours, and MPP+ (5 uM) increased DCF labeling by 34.5%. Also, H2O2 as well as MPP+ significantly decreased the number of tyrosine hydroxylase neurons by 51.3% and 46.6% 72 hours after treatment respectively. Ongoing, studies are evaluating the effects of monoamines in reversing or preventing the reported changes as well as their effects on antioxidant enzymes. The data from the ongoing studies will provide critical information prior to repeating these experiments in an in vivo model. In addition, the data from these studies will provide potential insight into the role that monoamines play in the neurodegenerative process.

Scopolamine, a non-selective muscarinic receptor antagonist, has recently been found to have rapid antidepressant effects, even in a subset of patients who are resistant to other treatments. Compellingly, women have a greater antidepressant response to scopolamine than men, an effect that suggests heightened female sensitivity to the drug. Most sex differences in drug efficacy are thought to be attributable to circulating ovarian hormones. To test whether scopolamine efficacy is regulated by ovarian hormones, we utilized rat models of antidepressant efficacy. First we found that in the Novelty Suppressed Feeding (NSF) test of antidepressant efficacy, scopolamine had a greater antidepressant effect in female than in male rats. Next using the NSF task we determined that the magnitude of scopolamine's efficacy changed across the estrous cycle. To further examine a role for circulating ovarian hormones we tested the effects of scopolamine in ovarietomized female rats utilizing NSF. Female rats were tested similarly. Effects of scopolamine in ovarietomized female rats utilizing NSF. Female rats were tested similarly. Effects of scopolamine in ovarietomized female rats utilizing NSF. Female rats were tested similarly.
Parkinson’s disease (PD) is a neurodegenerative disorder, characterized by the loss of dopamine neurons in substantia nigra (SN), with subsequent depletion of dopamine (DA) in the striatum. The cause of the loss of DA neurons in PD is unknown. However, oxidative stress has been suggested to play a role in the degeneration of DA neurons in the substantia nigra. The neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induces oxidative stress and loss of DA neurons in the substantia nigra, similar to the loss observed in PD. Previously, the lab has demonstrated that MPTP/MPP+ induces oxidative stress, dopamine depletion and nigra dopamine cell loss in vitro as well as in vivo. Fumaric acid (FM) has been demonstrated to increase astrocytes production and increase antioxidant enzyme expression. In the present study our objective was to 1) determine if fumaric acid decreases reactive oxygen species (ROS) produced by MPTP/MPP+ in nigra neuron/glia co-cultures 2) determine if fumaric acid prevents MPTP/MPP+ induced loss of dopamine neurons in nigra neuron/glia co-cultures. The results show that FM significantly reduced the production of ROS induced by MPP+. In addition, FM prevented mitochondrial dysfunction as well as loss of dopamine neurons induced by MPP+. The findings from these studies may offer insight into the mechanism of action of fumaric acid, and possible present as a new therapeutic strategy to treat neurodegenerative disorders such as PD.

Therefore, any non-linear interactions must be cortical and are likely mediated by GABA. We hypothesize that there are sex differences in the non-linear cortical interactions. The patterns used consisted of windmill-dartboards (WD) or partial windmills (PW) modulated at 4 Hz, presented for 2 seconds and repeated 10 times. The electrical activity of the brain was recorded and signal averaged to yield VEPs. We examined the fundamental and second harmonic components extracted by Fourier analysis of the recording. The VEP responses elicited by PW reveal a second harmonic which is greatly attenuated in response to WD (long range lateral interaction). WD elicited a prominent fundamental component not present in the PW (short range lateral interaction). This evidence for short and long range non-linear inhibitory mechanisms is consistent with previous findings. We found that females have overall larger amplitudes in all components of the VEP. However, there are no significant sex differences in the relative sizes of the amplitudes. Hence, males and females have very similar long and short range lateral inhibitory mechanisms.

MicroRNAs (miRNAs) are small, non-coding RNAs that post- transcriptionally regulate gene expression and have been implicated in drug addiction. We previously found that miR-495 targets several addiction-related genes and is downregulated in the nucleus accumbens (NAc) following acute cocaine administration. Here, we measured NAc miR-495 expression during cocaine self-administration (SA) and tested the functional role of NAc miR-495 by virus-mediated overexpression during cocaine and food SA. Rats were trained to lever press for cocaine (0.09 mg/kg/infusion) for either 1 or 22 days on a fixed ratio (FR) schedule of reinforcement, sacrificed one hour following their final session, and NAC tissue was dissected and processed using qRT-PCR. We found that NAC miR-495 levels decreased after 22, but not 1, day of SA. A separate group of rats were infused with a lentivirus into the NAC that overexpressed either green fluorescent protein (GFP; control) or GFP+miR-495 and were tested on a FR5 and progressive ratio (PR) schedule. NAC miR-495 overexpression decreased cocaine intake under a PR, but not FR5, schedule. We performed the same manipulation on a separate group of rats that were trained to lever press for food reinforcement and observed no effects on either schedule. Taken together, NAC miR-495 appears to be downregulated following prolonged, but not brief, cocaine SA and regulates genes involved in cocaine, but not food, motivation.
Negative symptoms, such as social withdrawal and flattened emotional affect, remain an unsolved problem in Schizophrenia. The fear and reward networks mediate many of these altered social and emotional behaviors, and are also dysregulated in schizophrenia.

Participants (n=61) are from 3 groups: Healthy controls (HC), individuals with schizophrenia (SZ), and individuals at clinical risk for psychosis (CR). Subjects underwent a passive fear conditioning task during 3T BOLD fMRI in which subjects learned to associate two faces with either an aversive auditory stimulus (CS+) or lack thereof (CS-), followed by a reversal paradigm in which the associations with both faces were reversed.

Relative to HC, CR and SZ showed decreased CS+>CS− difference from the acquisition run to the reversal phase in ventromedial prefrontal cortex (vmPFC). In the amygdala, the CS+>CS− difference was negatively correlated with negative symptom severity during reversal. Finally, activation to the neutral condition in the ventral striatum showed a positive correlation with negative symptom severity during reversal.

The vmPFC and amygdala play a critical role in fear learning, while the ventral striatum regulates reward. Our results from the acquisition run to the reversal phase in ventromedial prefrontal cortex (vmPFC) indicate that these regions are important in the reversal of learned fear, and that the schizophrenia pathology interferes with this reversal. This inability to properly reverse fear conditioning may underlie some of the most debilitating behavioral traits in schizophrenia such as social withdrawal and paranoia.

An estimated 1 in 68 children have an autism spectrum disorder (ASD). ASD is a neurodevelopmental disorder characterized by social and emotional impairments and repetitive stereotyped behaviors. Two dominant hypotheses about how social impairments arise in ASD propose that social interactions are either 1) less rewarding, or 2) produce increased anxiety. To date, these alternatives have not been directly examined in ASD model mice. Here we propose to modify an existing runway task that will allow us to measure putative social anxiety and reward phenotypes in the Fmr1 KO mouse model of Fragile X (FX), which is the most common form of ASD, accounting for 5% of cases, and is caused by a mutation in the FMR1 gene. Our novel task two social-alternative forced choice (2AFC) task will constrain the subject mouse to choose between two paths in order to traverse an open runway from one dark chamber to another. One path will contain a video of a social object facing forward (Ffso) while the other will have the same social object facing backward (Bfso). Pilot data shows that WT mice at ages p30 and p60 prefer the Ffso, and the phenotype is lost at age p90. An increased preference for the path containing the Bfso in the Fmr1 KO mice compared to wild type controls, will indicate social anxiety, while no preference will indicate diminished social reward. This assay will therefore allow us to distinguish between the two dominant hypotheses about how social impairments arise in ASD.

Parkinson’s Disease (PD) is a neurodegenerative disease that mainly affects the motor system. Impaired vesicular storage of dopamine is a feature of Parkinson’s Disease (PD) and genetic mutations in proteins associated with synaptic vesicles, can lead to PD. Synaptic vesicles play a crucial role in packing neurotransmitters, fusing with the membrane of pre-synaptic neuron and releasing the neurotransmitters in the synaptic space. The function of dopaminergic vesicles is regulated by the synaptic vesicle glycoprotein 2C (SV2C). SV2C is a vesicular protein enriched in basal ganglia and is a genetic modifier of Parkinson’s Disease (PD) risk in smokers. Our lab has previously shown that knocking out SV2C in mice (SV2C-KO) leads to a reduction in dopamine release and subsequent motor impairments. To investigate potential compensatory changes arising from this neurochemical change, we evaluated expression of various synaptic proteins. We found that SV2C-KO leads to a neurochemical change observed in SV2C-KO animals. We also examined potential alterations in non-dopamine transmitter systems (GABA, acetylcholine and glutamate). Finally, we examined whether SV2C-KO leads to a disruption in vesicular protein complexes within dopaminergic and non-dopaminergic transmitter systems. Thus this research will help us understand the contribution of alterations in non-dopamine transmitter systems in basal ganglia to neurochemical and behavioral alterations in SV2C-KO animals.

The mesolimbic dopamine pathway including the ventral tegmental area and nucleus accumbens (NAc) plays an important role in reward value processing, goal-directed behavior, and reinforcement learning. Specifically, midbrain dopaminergic neuron activity has been reported to encode a reward prediction error (RPE) to signify the need for adjustment in estimating current and future reward value. Pertinent to dopamine reward circuitry, patients with schizophrenia show dysregulation of dopamine in the striatum, along with deficits in motivation and cognitive performance. To evaluate the involvement of dopamine in reward prediction and motivated behavior, we created a transgenic mouse model resembling the increase in density and occupancy of striatal D2R observed in clinical schizophrenia. Our transgenic and control mice underwent chronic implantations of carbon-fiber microelectrodes in the core region of NAC to measure real-time dopamine release using in vivo fast-scan cyclic voltammetry. In a probabilistic operant conditioning task, animals were presented with auditory cues, which predicted a high (75%) or low (25%) probability of receiving a bigger reward (food pellets) prior to the reward delivery. We observe cue-reward associations are learned when dopamine release occurs in response to the cue that predicts reward, parallel to markedly increased anticipatory head entries to food receptacle in response to tones. Our preliminary data suggest that RPE sensitivity, reflected by dopamine release, is reduced in D2R-overexpressing mice. A reduction in RPE sensitivity, potentially due to striatal D2R overexpression, may underlie the impairments in motivation and cognition observed in schizophrenia.
Neuroscience, Psychology and Behavioral Sciences

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The In Vitro Culturing and Immunolabeling of the Kisspeptin-expressing Neurons to Investigate the Classical Progesterone Receptor

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Ovulation is caused by the LH surge, which is caused by estrogen positive feedback. Progesterone is an essential component of the LH surge. Rising levels of estrogen prior to ovulation increases progesterone receptor (PR) expression, yet the specific cells in which induction of PR occurs have not been identified. Here, we investigate whether classical PR is upregulated in kisspeptin neurons. We used mHypoA51 neurons which are immortalized cells derived from adult female mouse hypothalamus. These cells model kisspeptin neurons in vivo that govern the LH surge. We stimulated these neurons with 30 minutes of estradiol (E2) and compared PR immunoreactivity to untreated controls. We also used antibodies directed towards membrane progesterone receptors, mPR-alpha and mPR-beta, to examine potential non-classical progesterone signaling. In untreated mHypoA51 neurons, 95.2% expressed mPR-alpha, & 86.2% expressed mPR-beta. E2 treatment did not affect PR expression (61.8% control vs. 57.3 % E2-treated). Results indicate that mHypoA51 neurons are highly progesterone-responsive, as they express multiple receptors. While E2 has been shown to upregulate classical PR, the present results suggest that this upregulation requires longer E2 exposure. Further research is necessary to translate these in vitro findings in vivo.

Neurogenic pain is difficult to repair and alleviate. Pain is experienced through the integration of neuronal circuits involved with nociceptive signaling. These harmful stimuli are encoded and processed through a specific group of mechanosensory TRPA1 channels. Those who suffer from neuropathy-based pain attempt to relieve pain symptoms with prescription analgesic medications. Most of these medications come with detrimental side effects including a triggering of the brain’s reward and addiction pathways. Taking these drugs for an extended period of time results in dependency problems. In an effort to understand the neuropathological changes associated with neuropathic pain sensation and to understand how these channels respond during pain stimuli, I will closely examine the effects of suprathreshold stimuli on the TRPA1 channel and manipulation with the putative neuropathic analgesic, THC (delta-9-tetrahydrocannabinol). TRPA1 channel activity will be assayed using the zebrafish model through electrophysiological recording, behavior recording, and anatomic changes in TRPA1 neuron anatomy and connectivity. Specifically, I will use electrophysiological methods to record noxious signal modulation in zebrafish from the TRPA1 channel containing cranial nerve VIII while in the presence of THC.

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Understanding Noceceptor Triggering and Modulation in the Absence of Noxious Stimuli

Crystal Smith, Dr. Lisa R. Ganser

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Both number of objects (numerosity) and their complexity determine the capacity of visual short-term memory or VSTM (e.g., Alvarez & Cavanagh, 2004). A marker of the complexity dimension of VSTM capacity has yet to be isolated from electrophysiological activity in the brain. The goal of our study was to determine whether complexity dimension of VSTM capacity could be marked using proportional changes in event-related desynchronizations (ERD) of electrophysiological activity (Pfurtscheller, 1992, 2001) during retention. In our study, participants remembered arrays of Chinese characters that varied in complexity (3, 6, or 9 strokes) and numerosity (2, 3, or 4 characters). After a one second retention period, participants were instructed to indicate whether the displayed Chinese character was the same as or different from the characters shown in the previous screen. Intervals of catch trials (in which no stimuli were presented) were shown intermittently throughout the experiment to provide a baseline for our measurements. We found an effect of only complexity, and not numerosity, on the ERD measure. Analysis of behavioral data showed that participants’ accuracy decreased as a function of increase in both complexity and numerosity. Participants’ reaction times increased with increasing complexity, while numerosity had no effect. This data pinspoints a previously unexploited measure of VSTM which can be potentially used for detection and treatment of memory problems in children and adults.

The combined effects of ethanol and nicotine on the brain and on behavior was investigated, neurobiological features of zebrafish will be utilized in research. Studies indicate that combining ethanol and nicotine can produce rewarding effects that are greater than that produced by each drug alone. The aim of this experiment was to determine if low doses of ethanol and nicotine produced the same reinforcing response as a high dose of the individual drug. Zebrafish were conditioned to associate nicotine, ethanol and nicotine + ethanol combinations with distinct visual cues through a procedure involving classical Pavlovian conditioning. The low doses of each drug that did not produce rewarding effects were combined to measure the combined effects of both drugs. Subjects’ initial preference between two compartments with different visual cues was first tested. Zebrafish were exposed to drug in the less-preferred chamber of the test apparatus and then exposed to untreated aquarium water in the originally preferred side of the apparatus. These steps were repeated and on the test day zebrafish were placed into the apparatus with only aquarium water. This enabled comparison of the preference for the drug-paired compartment before and after conditioning. Behaviors were recorded and analyzed using EthoVision software. Data showed that zebrafish seemed to have an adverse effect to drug combinations similar to the effects seen with a high dose of an individual drug. These data suggests that combining low doses of ethanol and nicotine produces effects similar to those produced by high doses of one drug alone.

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Desynchronization Index: A Novel Marker of Visual Short-Term Memory Capacity

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Measuring the Rewarding Effects of Nicotine and Ethanol Polydrug Use in Zebrafish (Danio rerio)

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Nicotine and ethanol have been identified as two of the most abused illicit drugs in the United States. One of the anecdotally reported uses of nicotine is that it helps alleviate stress. However, nicotine’s mechanism of action involves dopaminergic release which can stimulate arousal and motor activity leading to anxiety-like symptoms. Ethanol acts as a depressant that increases GABA release to inhibit stimulation. Based on the neurotransmitters released by nicotine and ethanol, it would be likely that nicotine would increase anxiety while ethanol would decrease anxiety. Yet it has been estimated that over 83% of alcoholics also smoke and that alcoholism is approximately 10 times more prevalent in smokers than in non-smokers. In order to investigate the effects of nicotine and alcohol on anxiety, zebrasfish novelty-elicited responses following acute and chronic exposure to nicotine, ethanol, and a combination of both drugs were measured. Based on the high incidence of nicotine and alcohol co-dependence reported in epidemiological studies, we hypothesize that the nicotine + ethanol drug combination might produce anxiolytic effects. Typically, zebrasfish dive to the bottom of the tank when placed in a novel environment suggesting that this behavior might be an escape mechanism from predators and indicate anxiety. Behaviors measured included mobility, areas of exploration and distance moved.

WIC is an important community source for child health information for low-income families. Little is known about the role WIC plays in assessment of children at risk for developmental delays. 539 parents completed English or Spanish surveys at 10 Oregon WIC clinics. 153 Oregon WIC staff completed online surveys. Parent survey items assessed knowledge of normal and delayed child development and frequency of sharing developmental concerns with WIC staff. Staff survey items assessed knowledge of child development, frequency of parent and staff concerns about child development, and WIC connectedness with county Early Intervention/Early Childhood Special Education (EI/ESCE) and pediatric providers. Descriptive and multivariate statistics assessed parent knowledge about development and by race/ethnicity/language, frequency of parent sharing developmental concerns with WIC, frequency of WIC staff developmental concerns, and WIC staff connectedness with EI/ESCE and pediatric providers. Mean score on parent assessment of child development was 68% correct, with non-Latino white (NLW) families scoring higher than Latino families with limited English proficiency (L-LEP). Overall, 35% of parents reported sharing developmental concerns with WIC staff. L-LEP families and non-Latino other race families were more likely than NLW families to share developmental concerns 40% of WIC staff reported parents ask about developmental concerns > once per week; 28% of staff reported having concerns about a child’s development > once per week. Mean staff score on the child development assessment was 82%, indicating staff are knowledgeable of developmental delays. More staff reported feeling very well connected to EI/ESCE, and to all/almost all local pediatric providers.

Aspect refers to the different ways of viewing time-based characteristics of situations. Two types of aspect exist: grammatical and lexical. Grammatical aspect consists of two parts: imperfective and perfective. The imperfective form presents an event as in progress (e.g., rescuing); the perfective presents an event as completed or finished (e.g., rescued). Lexical aspect is divided into two parts as well: telic and atelic. Telic verbs denote an event with an inherent endpoint (e.g., rescue); atelic verbs denote an event without an inherent endpoint (e.g., watch). This study measured eye-fixation time while participants read sentences such as: ‘The fireman was rescuing the kitten in which verbs differed in grammatical and lexical aspect. When a telic verb is paired with the imperfective form (was rescuing), the end point is less obviously presented, and inherent endpoint is subtracted. When atelic verbs are paired with the perfective form (watched), a temporal boundary is added. The addition hypothesis states that if adding a temporal boundary to the representation of a temporally bounded event requires mental effort, then eye-fixation times for perfective forms will be longer for atelic predicates compared to telic predicates. The subtraction hypothesis states that if removing the endpoint from the representation of an inherently bounded event is costly, then eye-fixation times for imperative forms will be longer for atelic verbs compared to atelic verbs. Results supported the subtraction hypothesis and weaker support existed for the addition hypothesis. We discuss the implications of these results for theories of event cognition and language acquisition.
Particles falling through stratified density layers of fluids occur throughout the natural world and affect various aspects of life such as the formation of thin layers of marine aggregates in the ocean, pollution clearing times, and air quality. The experimental setup consists of a sphere falling through two layers of stably, sharply stratified corn syrup with matched viscosities. The top layer sits above the denser bottom layer and a sphere of higher density that both layers is dropped in this configuration. In this study, we sequentially change the bottom layer density to approach the density of the sphere, the experiment is filmed and the data is analyzed, which allows us to track the sphere’s position and velocity profiles. There are many difficulties when running these experiments including stratifying the layers sharply by diluting salts, matching the viscosities of the layers, as well as suppressing convection. These sets of experiments helps us understand the validity of the theory currently published by suppressing convection. These sets of experiments helps us understand the validity of the theory currently published by

Oceanic beaches are dynamic ecosystems that are constantly changing. One of the main sources of change on oceanic beaches is erosion resulting from winter storms and hurricanes. Erosional change can be combat by renourishment projects. During renourishment projects, sand is dredged from offsite locations and placed on the beach in the eroded areas. Recent studies have shown that both erosion and renourishment can affect the microbial species found on the beach. One important microbial species that is of concern on oceanic beaches is Escherichia coli, which can be an indicator of pollution and other pathogens. In this study, we examined how the process of renourishment affected the abundance and distribution of Escherichia coli on an oceanic beach. To do this, we collected sand samples from three sections of the beach (i.e. dunes, intertidal, sub-tidal) at 30 sites over a two-year period and examined how Escherichia coli varied spatially in presence and abundance across the beach. Using this approach, we determined that Escherichia coli was present in all locations across the beach, but was significantly influenced by renourishment. More specifically, we determined that there were significantly higher levels of Escherichia coli in the intertidal zone of the beach, which is where renourishment takes place. In addition, we also determined that the effects of renourishment were reduced over time, but not entirely diminished. Collectively, our findings indicate that renourishment has an effect on the abundance and distribution of Escherichia coli but, more work is needed to fully understand this process.

Community Led Total Sanitation (CLTS) is an intervention that strives to end the practice of open defecation. This study measured the effectiveness of CLTS in Nyando District by examining the association between community latrine usage and childhood diarrheal illness. A condensed cohort study design surveyed households with children 5 and younger to ascertain information on diarrheal illness, sanitation, and health behaviors. Water testing was conducted to determine E. coli and turbidity levels for 55 water sources in the locations. Anthropometric data was obtained for each child subject.

Data was obtained from 210 parents or caregivers in a 100% latrine community and 216 parents or caregivers in an open defecation free (ODF) community. The non-ODF had a nonsignificant 16% increase risk of diarrhea compared to the ODF community. Children’s HIV positivity (AOR=2.29; 95% CI: 2.07, 2.53), unsafe child stool disposal (AOR=9.2; 95% CI: 1.74, 2.12), and low household income (AOR=1.93; 95% CI: 1.46, 2.56) were all positively associated with diarrhea. The ODF location had a higher percentage of unsafe drinking water compared to the non-ODF location (67% vs. 60%). Diarrheal disease rates in children did not differ by whether a latrine intervention was implemented. Our findings suggest that water safety offset the relationship between ODF status and diarrheal status due to a higher likelihood of unsafe water consumption in the ODF community. Improved water treatment practices, safe stool disposal, and education may improve the CLTS intervention in ODF communities and therefore reduced the risk of childhood diarrhea.

There are stark differences in longevity between Black men and White men in the United States. As of 2010, the average life expectancy for White males was 76.5 years, whereas the average life expectancy for Black males was 71.8 years. Studies have also shown a vast difference in life expectancy between those who are in a higher social class than those who are not (in the year of 2000), the average life expectancy for the total population in the United States was 79.2 years for the most well-off individuals, whereas the least well-off individual’s life expectancy was 74.7 years. However, little is known about race differences among men of high social status. The objective of this study was to determine if there are racial disparities in longevity among elite NFL athletes. Our data includes key information on 250 All Pro Black and White NFL players from 1940 to 1969. Results show that both Black and White All Pro NFL players had similar life expectancies. On average, Black All Pro players’ first year in the NFL was about 8 years after that of White All Pro players’ first year. Black All Pro NFL players were more likely to play in the 1960s rather than the 1940s and the 1950s. Finally, after accounting for number of years All Pro, number of years played, Hall of Fame status, and the era in which they played, Black All Pro NFL football players had similar risk of longevity as White All Pro NFL football players.
Since September 2012, over 1700 cases of Middle East respiratory syndrome have been reported with over 85% of cases occurring in Saudi Arabia and a 36% case fatality rate. Dipeptidyl Peptidase 4 (DPP4), the only known receptor for MERS, is a multi-functional enzyme expressed on the surface of a variety of cell types and notably involved in blood glucose homeostasis. Type II diabetic people have dysregulated DPP4, and are at a higher risk for more severe Middle East respiratory syndrome-coronavirus (MERS-CoV) infection. Here, we hypothesize that there is a differential expression of DPP4 in the respiratory tract of type II diabetic patients that may lead to increased susceptibility, disease severity, and potential human-to-human transmission of MERS-CoV. Quantitative comparisons between type II diabetic and normal human respiratory tissues are done through mRNA transcription and protein expression analysis. Visualization of DPP4 mRNA and protein expression is done through in situ hybridization and immunohistochemistry on formalin fixed tissues. So far, we observe no significant difference in DPP4 expression between normal and type II diabetic human tissues via mRNA transcription analysis. A more inclusive set of human tissues and further experimentation is needed to determine DPP4 expression in the respiratory tract and potential for increased susceptibility and disease severity. Insight into the relationship of expression in the respiratory tract and potential for increased tissues and further experimentation is needed to determine DPP4 via mRNA transcription analysis. A more inclusive set of human tissues. So far, we observe no significant difference in DPP4 transcription and protein expression analysis. Visualization of normal human respiratory tissues are done through mRNA transcription and protein expression analysis. Background: In spinal fusion surgery, vision loss is a rare but damaging outcome commonly attributed to ischemic optic neuropathy (ION). This study analyzes trends in ION from 1998 to 2012 using the Nationwide Inpatient Sample (NIS) sponsored by the Agency for Healthcare Research and Quality. Methods: ICD-9 diagnosis and procedure codes were used to identify patients in the NIS that underwent spinal fusion procedures in the period from 1998 to 2012. Within this sample, national estimates of ION per three-year intervals were calculated using trend weights. Risk factors for incidence of ION were assessed using Poisson univariate and multiple regression models. Results: The estimated number of patients that underwent spinal fusion surgery from 1998 to 2012 in the United States is 2,511,073. Of these patients, 257 (1.02/10,000) developed ION. The number of patients with ION significantly decreased between 1998 and 2012 (Incidence Rate Ratio [IRR], 0.72 per 3 years; 95% confidence interval [CI], 0.58-0.88; P = 0.002). The strongest risk factors for ION were transfusion (IRR, 2.72; CI, 1.38-5.37; P = 0.004), age ten years (IRR, 1.24; CI, 1.05-1.45; P = 0.009), and obesity (IRR, 2.49; CI, 1.09-5.66; P = 0.038). The incidence rate of ION was lower in females compared to males (IRR, 0.30; CI, 0.16-0.56; P < 0.001). Conclusions: From 1998 to 2012, the number of ION in spinal fusion surgery has significantly decreased by a factor of 2.7. Risk factors for ION include transfusion, aging, obesity, and being male.

Polymeric nanoparticles (PNP) have the capability of direct cell access to the tumor cell due to size and the ability to attach ligands to target antigens on the tumor cell. PKS is a biodegradable polymer with increased biocompatibility compared to PLGA (poly lactic-co-glycolic acid), which is FDA approved for therapeutic devices. The goal of this research is to improve the properties of PKS for successful formation of PNP. To accomplish this study, increasing the molecular weight of PKS as a function of reaction time have been investigated for an overall size increase of the PNP. Additionally, endcaping PKS with sebacic acid was implemented to provide a more efficient attachment of the cancer targeting ligands to the PNP. 1H-NMR confirmed the successful synthesis of PKS by the appearance of the peaks at approximately 4.5 ppm. Increasing the reaction time also resulted in an increase in the peaks at 3.5 ppm that could be related to higher concentration of hydroxyl groups along the polymer backbone as function of increasing molecular weight. The successful formation of PKS endcapped with sebacic acid was demonstrated by the appearance of a peak at 11 ppm. ATR-FTIR also confirmed the successful formation of PNP polymers. Further analysis to confirm the changes in molecular weight as a function of time will be assessed using GPC along with nanoparticle size determinations by SEM.

Scavenger Receptor-A (SR-A) are cell surface receptors that are able to recognize different ligands including minimally modified low density lipoprotein (MM-LDL), enabling several biological functions like removal of foreign substances and waste materials in the body by specificity of extensive ligands via endocytosis, phagocytosis, adhesion, and signaling. One ligand for SR-A is dextran sulfate thereby allowing uptake of sulfated dextran-coated iron oxide (SDIO) nanoparticles by scavenger receptor-A, which is found on some cells present in the brain and spinal cord of the central nervous system. Previous research by the Louie lab has shown that there is an uptake of SDIO by scavenger receptor-A in activated microglia without significant levels of cytotoxicity. The iron-oxide content of SDIO nanoparticles make them a strong T2 MRI contrast agent, and their uptake by activated microglia suggest a possibility in their use in imaging brain inflammation. The objective of this study is to investigate the uptake and cytotoxicity of SDIO nanoparticles in astrocytes and neurons. If significant levels of cytotoxicity and uptake are found in non-microglia brain cells, it would hamper their use in imaging brain inflammation. Due to the cell density of astrocytes and neurons, determining the uptake via T2 measurements with a NMR relaxometer has been proven to be difficult from previous studies. This project involved developing an SDIO nanoparticle fluorescently tagged with a Rhodamine derivative in order to monitor the uptake via fluorescence.
Franzella tularensis is a Gram-negative coccobacillus and the causative agent of tularemia. Due to its low infectious dose, high virulence, and difficulty in diagnosis, an antigen capture ELISA is being developed for diagnosis of tularemia. A subclass switch of mouse immunoglobulin G (IgG) monoclonal antibodies with specificity to the lipopolysaccharide of F. tularensis was generated. Antibody-antigen interactions (binding affinity and specificity to the lipopolysaccharide of F. tularensis was generated using various fluorophores and imaged with confocal microscopy. Preliminary results using confocal microscopy revealed that receptor mediated endocytosis, as well as fluid phase macropinocytosis, were utilized by the DC 2.4 cells when exposed to antigens delivered by VAANA.

To meet the growing need for nanoengineered biocompatible materials to serve as cancer adjuvants, in this research, carbon nanotube arrays were fabricated by plasma enhanced chemical vapor deposition, followed by an alumina coating by the high yield and tightly controlled atomic layer deposition. These vertically aligned alinum nanowire arrays (VAANA) serve as a platform for delivering ovalbumin (OVA) to professional antigen presenting cells, dendritic cells (DC 2.4). The phycoschemical characteristics of VAANA significantly influences the delivery of OVA to these immune cells. The synthesized arrays were characterized by scanning and transmission electron microscopy. To investigate the effect of VAANA, the delivery efficiency of OVA was compared to a solution based delivery system, and qualitatively assessed by confocal microscopy and quantitated by flow cytometry. Further, the mechanism through which VAANA delivers the antigen and triggers cellular pathways was investigated using various fluorophores and imaged with confocal microscopy. Preliminary results using confocal microscopy indicate that the delivery efficiency using VAANA is higher than solution based antigen delivery. Confocal results indicate that receptor mediated endocytosis, as well as fluid phase macropinocytosis, were utilized by the DC 2.4 cells when exposed to antigens delivered by VAANA.

3D printing is a method of manufacturing which has been employed to create objects which via conventional methods is complicated or not possible. Recent efforts to print scaffolds in complex forms have been successful, although the appropriate cells have to be seeded and cultured on these scaffold susceptes to generate tissue. In the present case, an Agarose, MEM IX and HeLa cell mixture, dubbed Bio-Ink, was successfully created. This mixture allows cells to interact normally with agarose as the scaffold material while in the liquid state. The Bio-Ink gradually becomes a gel at optimal cell growth temperatures for effective printing. Cell proliferation and viability, after the HeLa cells have been subjected to heating and manual extrusion via a syringe, has been confirmed. Furthermore, an extrusion mechanism has been implemented in the 3D Printer which resembles a syringe pump mechanism. A 1 mm thick structure has been successfully printed using an Agarose mixture at 1.25% concentration. Larger structure are currently being printed with the Bio-Ink. Next, agarose will be substituted with a biodegradable material such as Chitosan and HeLa cells with human fetal osteoblasts. The growth of tissue generated by the osteoblasts is expected to eventually replace Chitosan in this process of engineering a solid tissue construct.

Variation in the zinc finger domain (ZFBD) of the protein PR Domain Containing 9 (PRDM9) is associated with altered placement of recombination in the human genome. As both the absence and altered placement of recombination are observed among chromosomes 21 that nondisjoin, we genotyped the PRDM9 ZFBD among Hispanic mothers of children with Trisomy 21 in efforts to determine if variation within this region, in comparison to a Caucasian and African populations, is associated with the recombinational risk for chromosome 21 nondisjunction (NDD). In our approach, PCR was used to amplify the ZFBD of PRDM9 and products were then subjected to bi-directional Sanger sequencing. DNA sequencing reads were aligned and compared to the sequence of the PRDM9 alleles previously identified by Berg et al. 2010. Chi-Square analysis was used to compare allele frequencies between cases and controls. Previous data shows that African male populations showed greater variation in the ZFBD of PRDM9 than their Caucasian counterparts (Berg et al, 2010). Based on this, we hypothesize that Hispanics will show a larger variation and more frequent occurrences of absent and altered placement of recombination at Chromosome 21 as compared to a Caucasian population. Data analysis revealed that there was no significant difference in allelic frequencies between the two populations.
Invasive species are a leading cause of worldwide biodiversity decline, with the Laurentian Great Lakes experiencing some 186 introductions. In ~1986 the Eurasian ruffe (Gymnocephalus cernua), a pike fish, was discovered in St. Louis Harbor, Lake Superior; about this time it also invaded Bassenthwaite Lake in northern England. The former was attributed to ballast water discharge from one or more transoceanic vessel(s) from the Baltic Sea region (according to our prior genetic data), while the latter was an apparent bait bucket introduction from southern England. The present investigation aimed to: (1) determine differentiation and diversity patterns between the invasive versus native ruffe populations, and (2) analyze whether their genetic compositions have changed over time, using 10 nuclear DNA microsatellite loci. Results indicate: (1) pronounced differentiation among the two invasive populations, with the native Baltic Sea and Great Lakes populations being similar, (2) both invasions likely were large with slight founder effects and different sources, (3) their genetic compositions have remained consistent over time (early 1990s-present), and (4) there is great genetic similarity across the current Great Lakes distribution, indicating range expansion of the initial colonists, without additional introductions. Native populations in the Baltic Sea region slightly differed (Vistula Lagoon versus Elbe River), with the latter genetically closest to the Great Lakes, indicating a likely founding source. This study demonstrates that population genetic analyses provide a robust and informative approach for discerning the temporal and spatial patterns of invasions.

Obesity is a major epidemic affecting the livelihood of many individuals. Attempts to control obesity by changing lifestyle has produced limited success. There is recent evidence showing that immune cells can regulate body fat, giving hope that the immune system could be manipulated to control obesity. Our study investigates the role of unconventional lymphocytes, (natural killer T (NKT) cells and double negative (DN) T cells) in regulating adipose tissue. Particularly, we analyze how the heparan sulfate proteoglycan, syndecan-1 (sdc1), can maintain body fat via control of homeostasis of NKT and DN cells in white adipose tissue (WAT) and brown adipose tissue (BAT). We hypothesize that sdc1 controls the cell number and function of NKT and DN cells in wild-type (WT) Balb/c mice and sdc1 knockout (KO) Balb/c mice. We predict in the absence of sdc1 there will be more NKT and DN cells which would negatively regulate body fat. To test our hypothesis, we isolated WAT and BAT from WT and sdc1 KO mice and analyzed with flow cytometry. Our results found more DN conventional T cells in W1 WAT than in sdc1 KO WAT. The DN T cell percentage was two times higher in WT tissue than sdc1 KO tissue. We isolated lymphocytes and analyzed with flow cytometry. Our results found more DN conventional T cells in W1 WAT than in sdc1 KO WAT. The DN T cell percentage was two times higher in WT tissue than sdc1 KO tissue. Additionally, double positive (DP) conventional T cells were higher in WAT than BAT (both phenotypes). Preliminary results suggest sdc1 may not play a regulatory role in conventional T cell populations. NKT cell populations must be studied further.

Epigenetic modifications of genomic DNA and the packaging proteins (histones) have the potential to modulate molecular profiles of organisms in response to changes of environmental signals. Recent studies have demonstrated the potential roles of DNA methylation to influence invertebrate phenotypes in the context of development, social roles, and diseases. Here we investigate how DNA methylation of the parasitic wasp Trichogramma pretiosum is altered due to intracellular parasitic bacterium Wolbachia. Specifically, in Trichogramma wasps, Wolbachia is transmitted vertically and induces parthenogenesis in females, a process in which unfertilized eggs develop into viable adult females. We analyzed whole-genome bisulfite sequencing maps of Trichogramma strains with and without Wolbachia infection. Hundreds of genes are differentially methylated between infected and noninfected strains, indicating substantial epigenetic changes accompanying Wolbachia infection. Interestingly, we identified numerous sites where DNA methylation changes are particularly drastic between the infected and noninfected strains. Characterizing epigenetic changes due to Wolbachia infection will enable us to gain insights into the mechanisms of parthenogenesis in Trichogramma and the consequences of a distorted gender ratio. Furthermore, understanding the epigenetic impact of Wolbachia infection can potentially improve the use of Trichogramma as a pest control agent.
Whooping cough is a highly contagious respiratory disease caused by Bordetella pertussis (Bp), affecting a rising number of infants nationwide. T Helper-17 cells are known to play a central role in the resolution of the infection, yet the bacteria’s toxins attenuate their response and delay their appearance until 15 days post infection. Our recent investigation into a pDC-derived IFNa-driven delay in this cell population’s response to infection has lead to a noted parallel rise of a T regulatory cell population secreting inflammatory IL-17 (~4% of total TH cells).

We hypothesize that, during whooping cough infection, Tregs develop a TH17-like effector phenotype when influenced by a TH17-polarizing environment in the lungs, moving from a defensive to offensive role. Flow cytometry analyses indicate these Tregs originate from the thymus (Helios+) and express regulatory markers such as CTLA-4 and PD-1. However, they also express trafficking markers and secrete inflammatory cytokines. Data from allogeneic system suggest that IFNa induce Treg-17 expression of a counterintuitive regulatory markers such as CTLA-4 and PD-1. However, they also express trafficking markers and secrete inflammatory cytokines.

Further analyses will interrogate the nature of these cells and evaluate their suppressor versus effector functions ex vivo. By uncovering the mechanisms that delay clearance of B pertussis, we hope to improve preventative approaches against this disease.
Background: Ehrlichiae are etiologic agents of febrile illnesses in humans and dogs, with a fatality rate up to 5%. These pathogens are transmitted by ticks, and infection is established following invasion of the white blood cells. Ehrlichia ewingii displays antigenic cross-reactivity with E. chaffeensis, but the surface protein antigens of E. ewingii are not characterized due to its non-cultivated status. Our project is developing approaches and tools to characterize the E. ewingii surface protein gene homologous to the major 120 kDa (gp120) diagnostic protein antigen of E. chaffeensis using a targeted RNA bait protocol.

Methods: A multiple sequence alignment was performed for the gp120 gene region of E. chaffeensis, E. canis, and E. muris using MEGAS4. Primers were designed for long-range tile amplification of 900-3,000 base pair fragments of E. chaffeensis. Several PCR protocols were tested for optimal amplification of target fragments and their identity was confirmed by sequencing.

Results: Optimized PCR conditions were established, and we amplified 5 overlapping fragments covering the target region and flanking genes. Each fragment was cloned into a plasmid, the recombinant plasmids were sequenced, and they were used as a template to generate biotinylated RNA baits. Our student led research entailed the use of established methods and the incorporation of new methods to cultivate and search for new antimicrobial compounds from collected soil samples. Once there was evidence of new compounds discovered, the research proceeded to identify, purify, and isolate potential organisms for further reproduction and study. New antimicrobials will lead the way in the fight against the ever increasing drug resistant strains of bacteria. A suspected soil sample that could contain new antimicrobial producers is serial diluted and plated to establish isolated colonies. Once isolated, a pure broth culture was grown from one of the colonies. After, the culture supernatants were then collected at different points of the growth cycle, establishing which growth phase produces the product. These potential antimicrobial producers were tested against ATCC Staphylococcus aureus and Escherichia coli strains with antimicrobials effective against Gram positive and negative bacteria to establish effectiveness. After testing various soil samples, a sample collected down river of a sewage treatment plant has shown to have antimicrobial activities. Further testing is underway using DNA sequencing, cloning and expression techniques to identify and categorize the bacteria and the antimicrobial present. This supports the idea that environmental conditions have a bigger role in soil bacterial diversity of activity.

Conclusions: These experiments demonstrated that RNA baits can be produced from PCR fragments of the Ehrlichia chaffeensis antigen gene. The baits will be used to optimize conditions for pull down experiments and recovering the homologous genetic fragments of E. ewingii from environmental and clinical samples known to carry this pathogen.
The impact of dehydration on several key physiological functions that are critical for athletic performance is well studied. Impaired physical functions has been suggested as a limitation on proper hitting technique in contact sports. Recently, there has been suspicion that recurrent poor contact technique can lead to an increased risk of injury, particularly mild traumatic brain injury. The purpose of this study is to investigate the correlation between hydration levels and head impact profiles of athletes, thus increasing an athlete’s susceptibility to mild traumatic brain injury. It is hypothesized that insufficient hydration levels will intensify head impact profiles of athletes, thus increasing an athlete’s susceptibility to mild traumatic brain injury. Urine specific gravity during preseason training at The University of Mississippi. Data tables are separated into three categories detailing hemoglobin A1c presence given percentages within the blood over a three-month period: normal (4%-5.6%), elevated (5.7%-6.4%) and abnormal (6.5%+). A sum of fifteen males and females are averaged together based on sex and A1c percentage to discern whether or not A1c levels within the blood are associated with increased or decreased weight loss between genders and persons without diabetes and those with diabetes. In conjunction to A1c levels, weight loss is measured in patients who documented to have regularly exercised as specified by the exercise therapist, used meal replacements as instructed by the nutritionist and have consistently participated towards successful completion of the study as recommended by the physician at the Johns Hopkins Weight Management Center. Results show that average A1c levels of patients without diabetes was notably lower than those with diabetes and weight loss in persons without diabetes was—on average—greater than those with diabetes, thus suggesting that persons with diabetes do experience slower rates of weight loss; however, a correlation between weight loss and A1c levels between genders was not significantly different. From a behavioral standpoint, research has shown that subjects without diabetes tend to successfully reduce their intake significantly more than diabetics, suggesting that differences in dietary adherence could in fact be responsible for the differences in weight loss.

Cyanine dyes consist of two terminal heterocyclic rings with nitrogen centers with one bearing a positive charge and are connected via an odd number polyethylene chain. With current synthetic methods, the conjugated system of the compounds can be altered to assume specific absorption and fluorescence spectra within the range of 400 to 1000 nm. Structural diversity is achieved by varying the polyene chain, the substituents on the nitrates and the heterocycles themselves. It is known that ligands with similar structural templates are able to bind with DNA via three main ways, including intercalative, groove, and external binding modes. As the negatively charged DNA surface attracts these electrostatically, the aromatic ring system of the compound can diffuse into the hydrophobic area between the DNA base pairs. Photodynamic therapy (PDT) is one of the medicinal applications of DNA intercalation. In PDT, when a photosensitizer is injected into the body and concentrates at the tumor site, it can be activated by light of a specific wavelength. Consequently, the cancer cells are killed selectively with minimal side effects. This therapy has been widely used as a treatment option for age related macular degeneration, acne, and cancer. However, recently we found a series of chromophores that can cleave DNA with various extent in the absence of light and/or an external reducing agent. It becomes crucial to investigate this property, because chromophores from this category automatically damage DNA without selectivity resulting severe side effects.

Sugar acids are monosaccharides with carboxyl groups. The main classes of sugar acids include Aldonic acids, Ulosonic acids, Uronic acids and Aldaric acids. Glucuronic acid is an example of a uronic acid that was first isolated from urine and is important for the metabolism of microorganisms. Glucuronic acid is also a component of the Onchocerciasis (riverblindness), a neglected disease biomarker N-acetyltetramine-O, glucuronid (NATOG). NATOG is a neurotransmitter- derived secreted metabolite from filarial parasitic nematode Onchocerca volvulus (Globisch et al 2013). These parasites are transmitted during a blood meal by a black fly vector (Simulium sp. carrying larvae, and affect more than 37 million people worldwide. Most infections occur in areas south of the Sahara Desert in Africa, Middle East, Central and now South America where there are limited resources for early detection and monitoring of disease. Current methods for early detection of the NATOG metabolite require specialized instrumentation, such as high performance liquid chromatography and mass spectrometry, which limit its use as a diagnostic biomarker. To circumvent this, an alternative rapid and inexpensive analytical tool is needed that would allow operation in these low resource settings. A two-component fluorescent system has been developed that utilizes a series of boronic acid receptors coupled to a fluorophore for quantification of sugar acids. The binding capabilities of the NATOG derivative glucuronic acid to six boronic acid receptors and the detection and quantification limits have been determined.
Liver receptor homolog1 (LRH-1) is an orphan nuclear hormone receptor that controls cholesterol and glucose metabolism, making it a promising target for treatment of metabolic diseases, such as cardiovascular disease and diabetes. Despite this therapeutic potential, the development of effective small molecule LRH-1 agonists has proved challenging due to a poor understanding of mechanisms governing regulation of the receptor by ligands. Moreover, present agonist design has been guided by a single crystal structure of LRH-1 with a synthetic compound. Unfortunately, a subsequent structure-activity relationship study based on the ligand position in this structure failed to improve efficacy substantially. Here, we present the crystal structure of LRH-1 bound to the lead agonist produced by ligands and offers insight into ways to improve agonist efficacy.

The glucocorticoid receptor is a ligand-regulated transcription factor that controls the expression of an extensive gene network, driving both up- and down-regulation. To control transcription, GR utilizes multiple mechanisms, both DNA-dependent and -independent, to achieve specific transcriptional outcomes. GR can bind directly to the DNA or GR can interact with other transcription factors through protein-protein interactions only. The latter mechanism, known as the tethering, has served as the only model of GR-mediated repression of inflammatory genes. However, ChIP-seq experiments have consistently shown GR to occupy AP-1 response elements (TREs), even in the absence of tethering factors. Therefore, the current model is insufficient to explain GRs action in these sites. We show that GR can directly bind the DNA at a subset of AP-1 response elements (TREs) in a sequence-specific manner and that transrepression at these sites is DNA-dependent. This expands GR’s mode of action allowing it to repress some TREs in the absence of AP-1 further expanding our understanding of this multifaceted transcription factor.
Vimentin is an intermediate filament protein that is used in the clinic as a biomarker for metastatic potential and poor patient prognosis across numerous solid tumor types; however, little is known about how vimentin might contribute to cancer metastasis. Here we created a novel genetically engineered mouse model (GEMM) to study the role of vimentin in lung cancer progression. In this model Kras/Lkb1 GEMM (termed KLV+/+) approximately half the mice that develop primary lung tumors in weeks also develop metastasis to the mediastinal lymph nodes. We used this model to test the hypothesis that vimentin loss worsens lung cancer metastasis by crossing this GEMM with a Vim−/− mouse to create a novel LSL-KrasG12D, LKB1H1F1, Vim−/− (termed here KLV+/−) mouse. Our findings show that in the KLV−/− mouse, primary tumor burden was not significantly different than wild-type KLV+/+ mice; however, KLV−/− mice exhibit significantly less metastasis to the mediastinal lymph nodes compared to their wild-type counterpart indicating that vimentin contributes to the metastatic cascade. Interestingly, vimentin staining in invasive regions of KLV+/+ mice was not found in the cancer cells but rather in fibroblast-like cells surrounding invasive cell buds termed collective invasion packs (CIPs). These fibroblast-like, vimentin-positive cells also stain positive for alpha smooth muscle actin, which is consistent with cancer-associated fibroblasts (CAFs). Taken together, these results suggest that in this highly metastatic genetic background, vimentin may play a central role in recruiting CAFs to invading cancer cells but not necessarily in cancer cell epithelial to mesenchymal transition (EMT).

Breast cancer is the most commonly diagnosed cancer among women in the U.S. Breast cancers with amplification and overexpression of the human epidermal growth factor receptor 2 (HER2) gene represent ~25% of metastatic cases. HER2 overexpression serves as a selective target for anti-cancer drugs. Trastuzumab was the first HER2-targeted therapy approved for the treatment of HER2-positive breast cancer. However, resistance to trastuzumab can develop in less than one year. One potential mechanism of resistance is the increased expression or compensatory signaling through receptor tyrosine kinases (RTKs), like the Insulin-like Growth Factor-1 Receptor (IGF-1R). Recently, we published data suggesting that cell invasion is a major biological outcome of IGF-1R and HER2 signaling in trastuzumab-resistant cells. However, among previous trials targeting IGF-1R in breast cancer, disappointing results have been observed possibly due to a crosstalk between IGF-1R and Insulin Receptor (IR), or the formation of hybrid receptors. Consequently, we propose a potential role for IR in the promotion of HER2-positive cell invasion. We want to determine if IR signaling can mediate invasion of HER2-positive cells, and if insulin stimulation of IGF-1R knockdown cells can restore invasiveness in the presence of trastuzumab. Preliminary results suggest that IR plays a role in cell invasion. Furthermore, insulin stimulation of IGF-1R-deficient cells treated with trastuzumab seems to restore the invasive potential of HER2-positive breast cancer cells. These results are the basis to a better understanding of trastuzumab resistance mechanisms in breast cancers with high IGF-1R/IR expression or signaling.

Plants are stationary organisms that must constantly respond to a changing environment in order to survive. Primary detection and response to flood stress occurs in the roots. However, how the specific cell types of the roots respond to these stresses is not completely understood. We have utilized two techniques, INTACT (Isolation of Nuclei Tagged in specific Cell Types) and TRAP (Tagged Ribosome Affinity Purification), to characterize the transcriptional and translational response of Medicago truncatula, alfalfa, roots to submergence stress. The nuclei and translating ribosomes are expressed in specific cell types of the root using Arabidopsis thaliana promoters. Our results show that all of the Arabidopsis promoters, with the exception of AtWox3, had the same localized expression in Medicago as in Arabidopsis. We also show that INTACT and TRAP can be performed using Medicago tissue. We are currently characterizing the response of alfalfa root cells to 2 hours of submergence stress. Our results will be compared to parallel experiments performed in tomato and rice in order to identify conserved genes involved in flood stress response in crops. The long-term goal of this research is to establish a comprehensive understanding of drought and flood stress response in crops and to use this information to develop harder crops.

Intellectual disability is the most common developmental disorder, with an estimated worldwide prevalence of 1%. Although in many cases the causes of intellectual disability are complex, a number of intellectual disabilities are caused by mutations in a single gene. The ZC3H14 gene encodes an evolutionarily conserved polyadenosine RNA binding protein, and loss of ZC3H14 expression leads to a form of inherited autosomal recessive intellectual disability. Loss of the ZC3H14 ortholog, dNab2, within Drosophila neurons impairs behavior, short-term memory, and alters patterns of axon guidance in the brain. Intriguingly, these brains exhibit longer poly (A) tails and increased levels of m6A (methylation of position-6 in the RNA base adenine) as compared to control flies. The m6A mark is an abundant and reversible, biologically relevance RNA modification linked to post-transcriptional gene regulation via diverse roles in mRNA processing. Biochemical data suggest that ZC3H14/dNab2 may interact physically with a metabolic enzyme known to deaminate adenosine monophosphate (AMP), leading to the hypothesis that this enzyme could act on m6A in RNA as well. Our preliminary data reveal strong genetic interactions between dNab2 and the AMP deaminase in a retinal model (GHR-dNab2). These preliminary studies will be followed-up with biochemical and genetic experiments to test the hypothesis that dNab2 controls m6A levels and expression of specific neuronal target RNAs by interacting with an AMP deaminase. These experiments could provide novel insight into how loss of ZC3H14 impairs brain function.
Humoral immunity is marked by long-lived antibody responses against pathogens. The duration of this response is dependent on long-lived plasma cells that are primarily located in the bone marrow and are of IgG isotype. However, we have identified a population of antigen specific, long-lived IgM plasma cells that reside in the red pulp of the spleen and display an atypical mutation profile. Following immunization of mice with 4-Hydroxy-3-nitrophenyl (NP) conjugated to chicken gamma globulin (CGG) (NPCGG) in alum, we isolated plasma cells (CD138+) and sequenced them via 454 pyrosequencing for µ heavy chain. Out of a total of 292 IgHV186.2 (which encode NP-specific antibodies) IgM sequences, we observe at least 58 that exhibited shared tracts of mutations (µ 3 mutations per tract). We find that these mutations are AID dependent and primarily occur in the framework regions of the VH gene - unlike IgG plasma cells, where mutations are predominately located within the complementarity determining regions (CDRs). Upon further analysis, we find strong evidence that these mutations appear to be shared between multiple unique IgM plasma cell clones isolated from different individual animals. Additionally, these tracts match other highly homologous VH genes in both position and identity. Taken together, we posit that these mutations in IgM plasma cell clones are not generated through murine somatic hypermutation pathways as described extensively in the literature but are, in fact, generated through templated mutation using highly homologous VH genes through gene conversion.

Many microbes have evolved to evade host adaptive immunity by coating their surface with mammalian-like antigens, a phenomenon known as molecular mimicry. Recent studies suggest that a class of innate immune factors, galectins, possess activity against these self-like microbes. However, while galectins typically recognize antigens that terminate in galactose, many microbes cap galactose residues with sialic acid. We sought to determine whether galectins maintain the ability to target sialylated microbes. Using the glycans microarray to examine the effect of glycan modifications on galectin binding, we found that Gal-8 (gal-8C) binds to sialylated galactose with high affinity vs its N-terminal domain (Gal-8N) specifically. This observed domain-specific affinity was reflected in whole-cell binding analysis of microbes, in which Gal-8 bound both sialylated and non-sialylated Group B Streptococcus (GBS), with Gal-8N preferentially binding to sialylated GBS, and the C-terminal domain (Gal-8C) binding exclusively to non-sialylated GBS. These findings suggest that Gal-8 may play a unique role in protecting against sialylated pathogens that self-modulate surface sialylation levels. Consistent with this hypothesis, incubation of Gal-8 with both strains of GBS results in loss of microbial viability as measured in colony forming units; while Gal-8N preferentially targeted sialylated GBS, Gal-8C selectively eliminated non-sialylated GBS. Together, these findings demonstrate that Gal-8 effectively targets both sialylated and non-sialylated GBS in a domain-specific manner. As modulation of surface sialic acid levels serves as a key virulence factor in several deadly sialylated pathogens, complementary antimicrobial properties of the individual Gal-8 domains equip Gal-8 as a unique protector against sialylated microbes.

Carbon dioxide pollution is among the top challenges facing contemporary society. The problem is compounded by the dependency of social progress on the very technologies that generate CO2, such as electricity generation, motor transportation, and certain industrial processes. This dependence makes it necessary to find ways of reducing CO2 pollution from such sources while maintaining the supply of those products and services. One such approach is carbon capture and sequestration (CCS), which targets high concentration point sources of CO2 pollution and uses chemical means to prevent the CO2 from entering the atmosphere. The major deficiency of current CCS technology is in irreversibility. The most successful materials used in CCS react with CO2 so strongly that it is difficult to separate the material from the captured gas. As a result it is necessary to deposit vast amounts of bound CO2 and capture material in nature creating a new environmental problem in the process. Our findings suggest that a class of innate immune factors, galectins, possess activity against these self-like microbes. However, while galectins typically recognize antigens that terminate in galactose, many microbes cap galactose residues with sialic acid. We sought to determine whether galectins maintain the ability to target sialylated microbes. Using the glycans microarray to examine the effect of glycan modifications on galectin binding, we found that Gal-8 (gal-8C) binds to sialylated galactose with high affinity vs its N-terminal domain (Gal-8N) specifically. This observed domain-specific affinity was reflected in whole-cell binding analysis of microbes, in which Gal-8 bound both sialylated and non-sialylated Group B Streptococcus (GBS), with Gal-8N preferentially binding to sialylated GBS, and the C-terminal domain (Gal-8C) binding exclusively to non-sialylated GBS. These findings suggest that Gal-8 may play a unique role in protecting against sialylated pathogens that self-modulate surface sialylation levels. Consistent with this hypothesis, incubation of Gal-8 with both strains of GBS results in loss of microbial viability as measured in colony forming units; while Gal-8N preferentially targeted sialylated GBS, Gal-8C selectively eliminated non-sialylated GBS. Together, these findings demonstrate that Gal-8 effectively targets both sialylated and non-sialylated GBS in a domain-specific manner. As modulation of surface sialic acid levels serves as a key virulence factor in several deadly sialylated pathogens, complementary antimicrobial properties of the individual Gal-8 domains equip Gal-8 as a unique protector against sialylated microbes.

Breast cancer is the leading cause of death among female cancer patients. ‘Human epidermal growth factor receptor 2 (HER-2) overexpression is associated with poor prognosis in 15-20% of breast cancer patients. Anti-HER-2 antibody (Herceptin) prolongs the survival of the HER-2+ breast cancer patients. However, resistance to Herceptin is a cause for relapse of aggressive, metastatic cancer in these patients. Our earlier studies have demonstrated that PD-L1 blockade enhances the efficacy of HER-2+ breast cancer whole cell vaccine by increasing the infiltration of T cells into the tumor. The goal of the present study is to determine the duration of protective anti-tumor memory responses to HER-2+ breast cancer. In this study, we demonstrate the beneficial effect of GPI anchored cytokine molecules as adjuvants for generating long lasting memory responses against HER-2+ as well as HER-2- breast cancer in syngeneic tumor models. Female BALB/c mice were challenged with D2F2/E2 (HER-2 transfected D2F2) cells or D2F2/E2 transfected with GPl-IL12 or GPl-GM-CSF. While the wild-type challenged mice developed tumors, the mice challenged with GPI- cytokine expressing D2F2/E2 cells were protected. Protected mice were re-challenged with D2F2/E2 cells 3 months later and D2F2/E2 cells 4 months later. All of the mice challenged with D2F2/E2 were protected. We have observed strong antibody responses against HER-2 and D2F2 tumor specific antigens in these mice. Our results show that long lasting protective anti-tumor memory response against D2F2 and D2F2/E2 is generated by vaccination with D2F2/E2 cells expressing GPI-anchored immunostimulatory molecules.
T cell function is tightly regulated by a fine balance of co-stimulatory signals, including those transduced by 2B4, an immunoglobulin-superfamily member induced on some T cell subsets. Recent studies from our group suggest that 2B4 plays a functional role in inhibiting donor-reactive CD8+ T cell responses in vivo, raising the possibility that 2B4 itself may be a therapeutic target to reduce allograft rejection. Thus, we hypothesized that augmenting 2B4 signaling would attenuate graft-specific CD8+ T cell responses following transplantation. To test this, we generated 2B4 retrogenic (2B4rg) donor-reactive CD8+ OT-I T cells that ectopically express 2B4. We found that constitutive 2B4 expression resulted in reduced accumulation of antigen-specific CD8+ T cells in the spleen 10 days post-transplantation. This was not due to differences in expression of the 2B4 ligand CD48 or CD8a in donor-reactive CD8+ T cells. Instead, we observed a marked reduction in the frequency of antigen-specific CD8+ memory T cells that express 2B4 following skin grafting. Pathogen-elicited memory T cells also expressed 2B4, albeit at lower frequencies (LM-OVA- 27%, gamma-Herpesvirus-OVA- 15%, and polyoma-OVA virus- 12%). We have shown that memory T cells elicited via these distinct antigen challenges pose differential barriers to graft survival following skin graft rechallenge in the presence of costimulation blockade (CD28-). Intriguingly, we identified a positive correlation (r=0.9943) between the MST and frequency of antigen-specific CD8+ memory T cells that express 2B4, suggesting that the presence of the 2B4 co-receptor molecule on T cells may render them more susceptible to a CD8a blocked regimen. Because the above results were done with Fc intact CD8+, we next queried whether Fc containing immunosuppression was required for the observed prolonged survival in wildtype relative to CD8a-/- mice. To accomplish this, WT and FcgRIIB-/- animals received skin grafts, and Fc-devoid a-CD28 domain antibodies (a-CD28 dAb) were substituted for CTLA-4-Ig. Similar to our observations in CTLA-4-Ig treated animals, a-CD28 dAb treated FcgRIIB-/- animals rejected their grafts more quickly than a-CD28 dAb treated WT animals (MST of 49 compared to 67 days), suggesting that the inhibitory effects of FcgRIIB are not dependent on Fc-containing drug regimens. Understanding the nature of endogenous ligands for FcgRIIB and how they are regulated during alloimmunity could illuminate novel, fundamental mechanisms by which humoral immunity may crossregulate memory T cell responses and also pave the way for development of a unique strategy to attenuate CD8+ allo-specific memory T cell responses following transplantation.

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FcgRIIB is an inhibitory Fc receptor present on B cells and other innate cells but not on T lymphocytes. Interestingly, we found that FcgRIIB-/- mice exhibit a marked reduction in antigen-specific skin graft rejection in the presence of CTLA-4-Ig relative to WT animals (MSTs of 20 and 33 days, respectively (P=0.0002)). To determine whether this increased rejection was due to enhanced donor-specific antibody, we analyzed recipient serum at day 20 post skin graft and found that DSA levels in FcgRIIB-/- mice were not increased relative to WT animals in the presence of CTLA-4-Ig. Because these data suggested that enhanced B cell responsiveness does not underlie the increased rejection observed in FcgRIIB-/-, we queried whether FcgRIIB is expressed on T cells during allografting. Surprisingly, we found that 80% of alloreactive cytotoxic-producing CD8+ T cells upregulated FcgRIIB following skin grafting. Pathogen-elicited memory T cells also expressed FcgRIIB, albeit at lower frequencies (LM-OVA- 27%, gamma-Herpesvirus-OVA- 15%, and polyoma-OVA virus- 12%). We have shown that memory T cells elicited via these distinct antigen challenges pose differential barriers to graft survival following skin graft rechallenge in the presence of costimulation blockade (CD28-). Intriguingly, we identified a positive correlation (r=0.9943) between the MST and frequency of antigen-specific CD8+ memory T cells that express FcgRIIB, suggesting that the presence of the FcgRIIB co-receptor molecule on T cells may render them more susceptible to a CD8a blocked regimen. Because the above results were done with Fc intact CD8+, we next queried whether Fc containing immunosuppression was required for the observed prolonged survival in wildtype relative to CD8a-/- mice. To accomplish this, WT and FcgRIIB-/- animals received skin grafts, and Fc-devoid a-CD28 domain antibodies (a-CD28 dAb) were substituted for CTLA-4-Ig. Similar to our observations in CTLA-4-Ig treated animals, a-CD28 dAb treated FcgRIIB-/- animals rejected their grafts more quickly than a-CD28 dAb treated WT animals (MST of 49 compared to 67 days), suggesting that the inhibitory effects of FcgRIIB are not dependent on Fc-containing drug regimens. Understanding the nature of endogenous ligands for FcgRIIB and how they are regulated during allografting could illuminate novel, fundamental mechanisms by which humoral immunity may crossregulate memory T cell responses and also pave the way for development of a unique strategy to attenuate CD8+ allo-specific memory T cell responses following transplantation.

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Recent research on the intestinal microbiota has demonstrated the importance of commensal microbes to host health. The question arises as to how commensals exert protective effects. Indoles are one such family of small molecules produced by some commensal bacteria and noted for their beneficial role in the health of diverse organisms. We hypothesize that indole-3-carboxylic acid (ICA), a model indole, modulates host damage tolerance, which is the capacity to endure stress without showing damage or disease. After lethal total body irradiation (12 Gy) is used to damage the intestine, ICA treatment extends survival and decreases the number of apoptotic cells in colonic crypts. We also found that daily administration of ICA (500 mg/kg) for two weeks alters the microbiota and allows for outgrowth of Akkermansia muciniphila, a mucus-degrading bacterium increasingly recognized for its anti-inflammatory and other protective functions. Increases in mucus production and the number of goblet cells per crypt in the colonic epithelium were evident by immunohistochemistry. Also, in vitro transepithelial electrical resistance studies show that ICA increases barrier function. Such changes may fortify the mucus barrier and preclude transplantation of bacteria and an injury to epithelia. Further studies will investigate the role of the aryl hydrocarbon receptor (AhR) and IL-22 in the changes induced by ICA treatment since indoles are known to activate the AhR pathway. Because these data suggest that ICA increases tolerance to injury, this could illuminate a mechanism for how the microbiota promotes intestinal health.

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SAMHD1 is an antiretroviral host restriction factor. HIV-1 relies on dNTPs to complete reverse transcription. SAMHD1 limits dNTP levels in macrophages and non-dividing cells by degrading dNTPs into deoxynucleosides and triphosphates. Low dNTP levels induced by SAMHD1 restrict HIV-1 infection in macrophages. Mutations in SAMHD1 have been associated with the genetic disorder Aicardi–Goutières Syndrome (AGS). AGS is an interferonopathy that mimics the symptoms of congenital viral infection and results in developmental delays. It is not known how SAMHD1 contributes to the AGS phenotype and the current mouse model used to study AGS does not exhibit AGS phenotypes. In order to determine whether C. elegans can be used as a model for studying AGS, we sought to characterize the activity of the C. elegans predicted SAMHD1 ortholog, ZK177.8 (cesAMHD1). First, we cloned the ZK177.8 gene and expressed the cesAMHD1 protein from E. coli. Next, we investigated the dNTPase activity of cesAMHD1 using an HPLC assay. The hydrolysis of dNTPs to dNs was observed upon the incubation with cesAMHD1, but only when co-incubated with dGTP or GTP. The dNTPase activity of cesAMHD1 was also confirmed by the TLC-based assay that used alpha-32P-dNTPs, which released triphosphate products. Indeed, as observed with human SAMHD1, the dNTP hydrolysis by cesAMHD1 also requires dGTP or GTP as a co-factor, and cesAMHD1 is unable to degrade NTPs and various nucleotide chain terminators. Finally, by using the cesAMHD1 knock-out THP-1 cell line, we are testing the ability of cesAMHD1 to lower cellular dNTP concentrations and restrict HIV-1 infection.

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Microbiology, Immunology and Genetics

Applications of Next-Generation Sequencing for Identification of Transmitted HIV-1

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The majority of heterosexual HIV-1 infections are initiated by a single variant, a transmitted/founder virus (TFV). TFVs can be inferred through high-fidelity amplification and sequencing of HIV-1 genomes from recently infected individuals and subsequent phylogenetic analysis. Here we employ next-generation, multiplexed sequencing with Pacific Biosciences (PacBio) to sequence near full-length genomes (NFLGs) of recently infected individuals. We amplified HIV-1 NFLGs from the plasma of eight HIV+ Zambians using a high-fidelity DNA polymerase. We then paired NFLGs with nucleotide barcodes to identify them in the multiplexed analysis. Thirty-nine barcoded NFLGs, including several previously sequenced with Sanger sequencing, were combined and sequenced with PacBio. Nucleotide reads generated by PacBio sequencing were analyzed with a MatLab code (Dilernia et al. 2015). A total of 35 sequences built from 60 reads and with >80% agreement per nucleotide position among the contributing reads were generated. Eight sequences were generated for NFLGs previously sequenced with Sanger sequencing; four of the eight were identical to the appropriate Sanger reference sequence. In the remaining four sequences, there was a median of two and range of one to six insertions/deletions/mutations in the PacBio sequences across the >9000 nucleotide Sanger reference sequences. Multiple NFLGs from an individual were sequenced to pursue TFV inference. Next-generation sequencing of barcoded NFLGs with PacBio permits high-throughput sequencing with high accuracy and at a lower cost (approximately $25 per genome) than Sanger sequencing. We have applied this technology toward inferring TFVs, which can be further studied for genotypic and phenotypic properties.

Since the first report of a plasmid-encoded phosphoethanolamine transferase gene conferring colistin resistance was described by Yi-Yun Liu and colleagues, mcr-1 has become an increasing concern due to the fears of rapid transferable resistance to our last resort antibiotics and the risk of global spread. Colistin is often the only therapeutic option available to treat infections caused by Gram-negative bacteria that are resistant to most or all classes of antibiotics. While a majority of studies have focused on retrospectively screening for the presence of mcr-1, fewer studies have focused on characterizing the full impact of mcr-1 within the context of the host. Here we report the first known study of mcr-1 conferring cross-resistance to the cationic host antimicrobial Lysozyme. Resistance to host antimicrobials may provide a selective advantage that could maintain and enhance the spread of mcr-1 carrying plasmids within the host in the absence of antibiotic pressure.

Microbiology, Immunology and Genetics

Transmissible Colistin Resistance Induced by mcr-1 Confers Cross-Resistance to the Cationic Host Antimicrobial Lysozyme.

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Clotridium difficile causes approximately 453,000 infections each year in the United States, leading to more than 28,000 deaths annually in the U.S. C. difficile infections typically arise after administration of antibiotics, and account for about 20% of all antibiotic-associated diarrhea. Antibiotics alter the normal intestinal microbiota, making the host more susceptible to C. difficile infection. In addition to the commensal flora, the host’s immune response is critical for warding off infection. The production of antimicrobial peptides (AMPs), such as LL-37, in the intestines provides a defense against many intestinal pathogens. Because of their broad-spectrum activity, AMPs are attractive targets for therapeutic development. However, due to the universal presence of AMP resistance mechanisms, new AMPs and AMP derivatives must be discovered and developed. The phoQ gene, which is highly induced in C. difficile in the presence of LL-37, is transcriptionally regulated by the PhoQ two-component system. Here we report the first known study of mcr-1 conferring cross-resistance to the cationic host antimicrobial Lysozyme. Resistance to host antimicrobials may provide a selective advantage that could maintain and enhance the spread of mcr-1 carrying plasmids within the host in the absence of antibiotic pressure.

Microbiology, Immunology and Genetics

An ABC-transporter Mechanism Confers Resistance to the Host Antimicrobial Peptide LL-37 in Clostridium difficile.

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Subpopulation

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Antibiotic resistant infections are a significant and increasing cause of morbidity and mortality. In particular, infections by multi-drug resistant Gram negative bacteria have commonly used classes of antibiotics are of particular concern, as the antibiotic colistin is often the only remaining treatment option. We have identified a multidrug resistant clinical strain of Enterobacter cloacae that is heteroresistant to colistin. This heteroresistant strain harbored coexistin colistin resistant and susceptible subpopulations that were genetically identical yet transcriptionally distinct. The colistin resistant subpopulation increased during antibiotic treatment, receded to baseline after subculture without drug, and was distinct from persisters. Presence of the resistant subpopulation was dependent on the histidine kinase gene phoQ. Antibiotic therapy failed to rescue mice infected with the heteroresistant strain, however antibiotic treatment of mice infected with the phoQ mutant was successful. Furthermore, an unrelated colistin heteroresistant E. cloacae strain with a resistant subpopulation that was undetected by clinical testing also led to treatment failure during colistin therapy. These results highlight heteroresistance as a cause of unexplained treatment failures and emphasize the need for novel therapeutics and diagnostics.

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Background: In the United States, HIV/AIDS disproportionately impacts racial/ethnic minorities. The US National HIV/AIDS Strategy (NHAS) aims to reduce these disparities. We describe and evaluate trends in the Black-White and Hispanic-White disparities of new AIDS diagnoses from 1984 to 2013 in the US.

Methods: AIDS diagnosis rates by race/ethnicity for people ≥13 years were calculated using US national HIV surveillance and Census data. Black-White and Hispanic-White disparities were measured as rate ratios. Joinpoint Regression was used to identify time periods across which to estimate rate-ratio trends. We calculated the estimated annual percent change (EAPC) in disparities for each time period using log-normal linear regression modeling.

Results: Black-White disparity increased from 1984-1990 (EAPC=5.6, p<0.01), followed by a large increase from 1991-1996 (EAPC=11.6, p<0.01) and a smaller increase from 1997-2001 (EAPC=3.2, p<0.04). Black-White disparity moderated from 2002-2005 (EAPC= -3.0, p=0.15) and rose again from 2006-2013 (EAPC=1.9, p=0.01). Hispanic-White disparity increased from 1984-1990 (EAPC=4.5, p<0.01), but declined after 1998 (EAPC= -1.2, p<0.01). Black-White and Hispanic-White disparities increased for MSM during 2008-2013 (EAPC (B-W)=6.0, p<0.01; EAPC (H-W)=3.3, p<0.01).

Conclusion: Recent increases in racial/ethnic disparities of new AIDS diagnoses were observed and may be due in part to care continuum inequalities. To monitor NHAS goals, we suggest assessing disparities in AIDS diagnoses as a high-level measure to capture changes at multiple stages of the care continuum collectively. Future research should examine determinants of racial/ethnic differences at each step of the continuum to better identify characteristics driving disparities.

Quantifying Isobutane Leakage Rates From Binary Geothermal Power Plants

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In a binary system, hot water is pumped from a geothermal reservoir and passed through a heat exchanger. The heat is delivered to a secondary working fluid with a lower boiling point than water such as pentane or isobutane. The secondary fluid vaporizes, powering the turbine and produces electricity. Because of the closed loop design, greenhouse gases dissolved in the geothermal fluid never interact with the atmosphere, resulting in a “near zero” emission claim. Many binary plants utilize organic working fluids, and can emit these fluids due to leakages and equipment breakdowns. The 2015 Paris agreement pushed for cleaner energies, including geothermal. Although geothermal power plants emit significantly less greenhouse gases than coal or natural gas plants, quantifying the emissions of isobutane is necessary as geothermal energy is utilized more in the future. Calculating isobutane emission rates is also useful to better compare emissions to other forms of renewable energies and fossil fuel based facilities for environmental impact.

The Effect of Hydroxylation on Anthocyanin-based Dye Sensitized Solar Cells

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Dye sensitized solar cells (DSSCs) have received intense scrutiny in recent years because of their significance as a simpler and cheaper generation of solar cells. This research focuses on a class of molecules called anthocyanins as the sensitizer. Anthocyanins are multi-cyclic organic molecules that are abundant in nature [1]. In this study three specific anthocyanins are under investigation, cyanidin, delphinidin, and pelargonidin. The three anthocyanins differ by the number and placement of hydroxyl functional groups. This study determined if these small differences affect the maximum current and voltage output of a DSSC constructed with these anthocyanins as the sensitizer. Electronic absorption spectroscopy was utilized to determine the maximum wavelength of absorption for each dye. The molar absorptivity of each dyes was determined through a Beer’s Law study and then a voltmeter was used to measure the voltage output of the DSSC with the assorted dye prepared.

Potential CXCR4 antagonists

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Chemokine receptor type 4 (CXCR4) is a cell surface receptor responsible for bone-marrow myelopoiesis, cardiac ventricular septum formation, and B-cell lymphoiesis. CXCR4 is important when cells migrate during inflammation and has been linked to various disease pathways such as cancer metastasis, inflammation disease, HIV-1 proliferation, and auto-immune disorders. CXCR4 along with its cognate ligand CXCL12 have been projected to regulate metastases sites in invasion of breast cancer cells. We have synthesized several pyridine and thiophene derivatives that have shown potential as effective CXCR4 antagonists.

Synthesis of Thiophene and Pyridine Derivatives as Potential CXCR4 antagonists

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Potential CXCR4 antagonists are projected to regulate metastases sites in invasion of breast cancer cells. We have synthesized several pyridine and thiophene derivatives.

The Effect of Hydroxylation on Anthocyanin-based Dye Sensitized Solar Cells

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Dye sensitized solar cells (DSSCs) have received intense scrutiny in recent years because of their significance as a simpler and cheaper generation of solar cells. This research focuses on a class of molecules called anthocyanins as the sensitizer. Anthocyanins are multi-cyclic organic molecules that are abundant in nature [1]. In this study three specific anthocyanins are under investigation, cyanidin, delphinidin, and pelargonidin. The three anthocyanins differ by the number and placement of hydroxyl functional groups. This study determined if these small differences affect the maximum current and voltage output of a DSSC constructed with these anthocyanins as the sensitizer. Electronic absorption spectroscopy was utilized to determine the maximum wavelength of absorption for each dye. The molar absorptivity of each dyes was determined through a Beer’s Law study and then a voltmeter was used to measure the voltage output of the DSSC with the assorted dye prepared.

Potential CXCR4 antagonists

Suazette Mooring
Department of Chemistry, Georgia State University, Atlanta, GA

Chemokine receptor type 4 (CXCR4) is a cell surface receptor responsible for bone-marrow myelopoiesis, cardiac ventricular septum formation, and B-cell lymphoiesis. CXCR4 is important when cells migrate during inflammation and has been linked to various disease pathways such as cancer metastasis, inflammation disease, HIV-1 proliferation, and auto-immune disorders. CXCR4 along with its cognate ligand CXCL12 have been projected to regulate metastases sites in invasion of breast cancer cells. We have synthesized several pyridine and thiophene derivatives that have shown potential as effective CXCR4 antagonists.
Saturated carboxylate homoleptic chains have been used as ligands and have had low melting thermotropic mesophases. 1 The homoleptic copper (II) dimer bridged by the branched 2-ethylhexanoate was synthesized as well as heteroleptic copper (II) dimers bridged by 2-ethylhexanoate as one or two of the four ligands. The other two or three carboxylate ligands included one of either octanoate, butanoate, hexadienoate, and benzoate. Only two different ligands including 2-ethylhexanoate were used per heteroleptic dimer. Caprolactam adducts were synthesized of either octanoate, butanoate, hexadienoate, and benzoate. Several chiral diamine ligands will be designed and synthesized, then applied to the selected organic reactions, such as hydrogenation of ketones and phosphonate derivatives. These chiral diamine ligands will be created in the lab from conception then made by using various techniques learned from literature. The chiral diamine ligands will be a new formulation that has not been explored. The usage of a TLC plate to monitor reaction progress, flash chromatography column to purify the products (HPLC), and instruments to analyze the structure of the products (NMR), are all vital to the success of this research. The synthesis of chiral compounds with high enantioselectivity is a challenge. In this research, the development of an efficient catalyst for asymmetric synthesis of a series of chiral products, which are potentially used as chiral intermediates for biologically active compounds will be conducted. These products then can be used to make life-saving pharmaceuticals. These catalysts can also be used in organic chemistry research to find more efficient methods to make known biologically active compounds. This research technique and application are still new and need to be investigated.

Asymmetric Organic Reactions

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Chemistry and Physics

Synthesis of Chiral Diamines and Their Use as Ligands for Transitional Metal Catalyzed Asymmetric Organic Reactions

Seth R. Fernandez, Qian Liang, Junpeng He, Bukuo Ni

Several chiral diamine ligands will be designed and synthesized, then applied to the selected organic reactions, such as hydrogenation of ketones and phosphonate derivatives. These chiral diamine ligands will be created in the lab from conception then made by using various techniques learned from literature. The chiral diamine ligands will be a new formulation that has not been explored. The usage of a TLC plate to monitor reaction progress, flash chromatography column to purify the products (HPLC), and instruments to analyze the structure of the products (NMR), are all vital to the success of this research. The synthesis of chiral compounds with high enantioselectivity is a challenge. In this research, the development of an efficient catalyst for asymmetric synthesis of a series of chiral products, which are potentially used as chiral intermediates for biologically active compounds will be conducted. These products then can be used to make life-saving pharmaceuticals. These catalysts can also be used in organic chemistry research to find more efficient methods to make known biologically active compounds. This research technique and application are still new and need to be investigated.


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Department of Chemistry, Knox College, Galesburg, IL

Chemistry and Physics

Comparing Macroporous Resin Performance in the Extraction of Anthocyanins from Aronia Mitschurini Berries

Adaobi S. Eguagu, Francisco Garcia, Davita Camp, Suazette Mooring, Taiwo Ola

Aronia Mitschurini, commonly known as the Black chokeberry, is a fruiting bush native to the East Coast of the US and cultivated as a specialty food crop in Eastern Europe. A close relative of the apple, it produces small, round berries with deep purple skin and flesh. Aronia berries contain a cocktail of antioxidants in significantly higher concentrations than Acai berries. The most notable of these compounds are anthocyanins. Responsible for giving the berries their deep red color and acting as a potent free radical scavenger, anthocyanins exists in the juice as well as the pulp. It has high value both in nutritional and technical applications.

Recently, polymeric/macroporous resins have been used to extract additional antioxidant values from Aronia melanocarpa and similar fruits. Extracted antioxidants can be used in health supplements, food products, colorant formulas, and possibly in the future as medication ingredients.

This project tested a current resin technique, on the extraction of anthocyanin from Aronia juice. The resin beads were first soaked in aronia juice. Once the anthocyanin molecules adsorbed to the vast internal surface area of the beads, the beads were removed from the solution and exposed to a solvent where anthocyanin was released from the resin. Anthocyanin and flavonoid concentrations before and after resin treatment and comparison of different resins will be presented.

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Department of Chemistry and Physics, Maryland Eastern Shore, Princess Anne, MD; University of Maryland Extension, Wye Research & Education Center, Queenstown, MD

Design and Synthesis of Heterocyclic Aromatic Based CXCR4 Modulators

Theresa Gaines, Gregory Adodo, Davita Camp, Suazette Mooring, Andrew G. Ristvey, Victoria V. Volkis

CXCR4 is a chemokine receptor that has been linked to several disease pathways including: HIV-1 proliferation, autoimmune disorders, inflammatory disease and cancer metastasis. The interaction of the C-X-C chemokine receptor type 4 (CXCR4) with C-X-C chemokine ligand 12 (CXCL12) plays an important role in triggering the aforementioned disease related pathways. Various antagonists for these receptors have been synthesized and tested, but many are not useful clinically either because of toxicity or poor pharmacokinetics. Some of the most extensive CXCR4 antagonist libraries have been based off of p-xylyl-enediamine compounds which all feature a benzene ring as the core of the compound. This work focuses on the design and synthesis of a new class of compounds that show potential as CXCR4 antagonists by using heterocyclic aromatic rings as the core scaffold. After synthesis, these aims will be probed through docking assays. So far this work has produced eighteen hit compounds based off of the 2,6-pyridine core, the 2,5-furan core, the 2,6-pyrazine core and the 3,4-thiophene core. These compounds have been a promising start to building a new library of CXCR4 antagonists.

Poster Presentations

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Chemistry and Physics

Synthesis and Characterization of Homoleptic and Heteroleptic Liquid Crystal Dimers Using 2-Ethylhexanoate as Main Ligand

Alejandro Beltran, Thomas W. Clayton, Jr.

Department of Chemistry, Knox College, Galesburg, IL

Synthesis and Characterization of Homoleptic and Heteroleptic Liquid Crystal Dimers Using 2-Ethylhexanoate as Main Ligand

Saturated carboxylate homoleptic chains have been used as ligands and have had low melting thermotropic mesophases. The homoleptic copper (II) dimer bridged by the branched 2-ethylhexanoate was synthesized as well as heteroleptic copper (II) dimers bridged by 2-ethylhexanoate as one or two of the four ligands. The other two or three carboxylate ligands included one of either octanoate, butanoate, hexadienoate, and benzoate. Only two different ligands including 2-ethylhexanoate were used per heteroleptic dimer. Caprolactam adducts were synthesized of either octanoate, butanoate, hexadienoate, and benzoate.

This project involves synthesizing chiral porphyrins by attaching (S)-(-) 2, 2-diamino-1, 1-binaphthalene and (R)-(+)-2,2-diamino-1,1-binaphthalene to porphyrin isocyanate, in order to improve the selectivity of the host in its chiral guest binding properties. One of the aims of the project is to mimic biological molecules in the body. Biological molecules such as proteins exist as chirally pure single enantiomers which selectively recognize chiral substrates or selectively catalyze the biosynthesis of single enantiomer chiral products. In this report, host-guest complexes of chiral or selectively catalyze the biosynthesis of single enantiomer chiral products. In this report, host-guest complexes of chiral or selectively catalyze the biosynthesis of single enantiomer chiral products.

The main goal of the project is to examine how the kinetics of proteolysis under acidic conditions (non-enzymatically and enzymatically by HIV-1 protease) depend on substrate length. Previous works using serine and aspartyl proteases indicate that the rates of ester, amide, and peptide bond hydrolysis increase with increasing substrate chain length (1, 2). An observed increase in proteolytic activity was also found when long-chain substrates were used under mildly basic non-enzymatic conditions, suggesting even more strongly that the increases were due to the substrate length (3). To investigate this, we have been synthesizing a series of homologous oligopeptides of varying lengths. The synthetic approach includes a combination of reactions (acylation, Fischer esterification, and peptide bond formation using conventional coupling agents). For example, acetylation of leucine and two dipeptides was performed to give the intermediates Ac-Gly-Gly-OH, Ac-Gly-Leu-OH, and Ac-Leu-OH. Fischer esterification was then used to synthesize Ac-Leu-OMe and it showed that the reaction runs slowly under the current conditions. Conventional peptide bond-forming reactions to synthesize targets like Ac-Gly-Gly-Phe-OMe are currently being attempted. Examples of the coupling reagents that have been used are CDI (N,N′-carbonyldimidazole) and pivaloyl chloride (PivCl). The kinetics analyses should provide information that can be used to better understand reaction mechanisms of protein strands and the relationship between substrate chain length and the rates of hydrolysis in protease systems.

Previous works using serine and aspartyl proteases indicate that the rates of ester, amide, and peptide bond hydrolysis increase with increasing substrate chain length (1, 2). An observed increase in proteolytic activity was also found when long-chain substrates were used under mildly basic non-enzymatic conditions, suggesting even more strongly that the increases were due to the substrate length (3). To investigate this, we have been synthesizing a series of homologous oligopeptides of varying lengths. The synthetic approach includes a combination of reactions (acylation, Fischer esterification, and peptide bond formation using conventional coupling agents). For example, acetylation of leucine and two dipeptides was performed to give the intermediates Ac-Gly-Gly-OH, Ac-Gly-Leu-OH, and Ac-Leu-OH. Fischer esterification was then used to synthesize Ac-Leu-OMe and it showed that the reaction runs slowly under the current conditions. Conventional peptide bond-forming reactions to synthesize targets like Ac-Gly-Gly-Phe-OMe are currently being attempted. Examples of the coupling reagents that have been used are CDI (N,N′-carbonyldimidazole) and pivaloyl chloride (PivCl). The kinetics analyses should provide information that can be used to better understand reaction mechanisms of protein strands and the relationship between substrate chain length and the rates of hydrolysis in protease systems.
We present a multi-epoch, high resolution study of ultraviolet interstellar C I absorption line profiles taken by the Hubble Space Telescope. The 17 stars of this survey were chosen because each has spectra taken at least 10 years apart with the same instrument, grating, and aperture. Given the proper motions and distances of these stars, typically it was possible to observe variations in their absorption line profiles which correspond to structure on scales of less than 200 AU. In the 17 sightlines no significant differences in C I line profiles between the two epochs were detected. A measurement of ~ 5% of sightlines with variances is consistent with the fraction found by McEvoy et al. (2015) in their much larger survey of multi-epoch variance of Na I. However, the sky exhibits variations at an LSR velocity of -37 km/s indicative of structure on scales of less than 200 AU. Interestingly, the sky shows significant variance in its C I line profile. The C I absorption arising from the J = 1 and J = 2 fine-structure states toward this star exhibits variations at an LSR velocity of ~73 km/s indicative of structure on a scale less than 200 AU. Interestingly, the sky position of HD 210809 corresponds to the edge of an interstellar H I shell discovered by Suad et al. (2012) at this same LSR velocity. This connection is consistent with the optical survey of interstellar Na I by Meyer et al. (2015) who found that nearly all of their temporally varying sightlines involved supernova remnants, H I supershells, or stellar bow shocks.

Tectonic processes, such as subduction and mantle flow, have been advanced over many years of research, yet our ideas on how these processes work are usually constrained to be simple 2-D models. Over that past 10 years, EarthScope, a National Science Foundation funded facility, has deployed various instruments across North America with the goal of gaining fundamental insight into how the Earth operates through imaging the crust to the core. One component of the facility is USArray, a rolling array of 400 seismometers with 70 km spacing that has covered the entire continental U.S. Because of the unprecedented seismic data collection, many new crust and mantle models of the U.S. have been developed by many researchers, and each are revealing unique, 3-D features. Thus, the typical 2-D tectonic working models on tectonic processes no longer match the new images being developed. We focus on correlating multiple data sets from a variety of sources from the Incorporated Research Institutes for Seismology (IRIS), the United States Geological Survey (USGS), and NASA. In particular, we correlate gravity, crustal thickness, seismicity, and topography to the new, averaged tomographic velocity models to identify the impact of deeper mantle structure on surface processes, in particular topography and faulting. We find topographic lows in regions of thinner crust that correlate with deeper, high velocity mantle anomalies (100-200 km), suggesting micro-downwelling (3-D flow) impact topography. We also suggest that persistent high velocity anomalies in the upper mantle may have created the Big Bend along the San Andreas Fault.

In April 2014, the city of Flint, Michigan changed their water source from treated Detroit Water and Sewerage Department water to the Flint River. After the change, residents began complaining about discoloration and the water’s taste and smell. From June 2014 to November 2015, 87 cases, 10 fatal, of Legionella bacteria were confirmed within the city’s radius. The events caused our team to wonder whether this crisis, and those in the future, could be avoided. A modern and innovative method for predicting epidemics has been to use crowd behavior data analytics as well as social media. Social media, especially Twitter, has played a prominent role in public health events, such as tracking an ailment over time and geography. Data is collected from free APIs provided by Twitter and read through R Programming software. A twitterR package is used to filter this data and focus on a particular time and sentiment. The data is then used in a tangible way to determine whether one could have predicted the Flint Water Crisis through analyzing twitter phrases.

Our current utility grid is outdated, over-engineered and it will soon be too archaic to meet our ever-growing energy needs. A solution to that issue is the Smart Grid, a completely digitized version of our present grid, which is comprised of mostly hardware. The Smart Grid would allow for two-way communication between producers, end users and every party involved in the process of generating, delivering and consuming energy. However, along with the implementation of the Smart Grid would come a plethora of security concerns that could arise from the manipulation of transmitted information. Our project addressed these types of security matters by employing an encryption algorithm that would ensure that the proper data is being transferred between the service provider and the consumer, and vice versa.
Schistosomiasis, also known as snail fever, is a disease transmitted by several species of flatworms that are carried by freshwater snails. The primary goal of the present work is to model disease progression using systems of nonlinear ODEs. The model follows the dynamics of both parasite and immune components. Parasite components considered are larvae, immature worms, mature worms, and eggs. Immune components modeled are resting macrophages, active macrophages and T lymphocytes (T-Cells). We investigate the sensitivity of the model with respect to relevant parameters like rate of granuloma formation, the number of eggs, the proliferation rate of the T-cells, etc. Our findings indicate a saturation in the value of the T-cell population as a function of the rate of granuloma formation. We find that the T-cell population diverges when the ratio of proliferation to death rates exceed a certain threshold value. We then use the Quasi Steady State Approximation (QSSA) to derive two reduced models of schisto-immune dynamics. We compare the behavior of the reduced models to the behavior of the original system. In each case, a linear stability analysis is done. We conclude that the endemic steady states for two of our models are stable, while the corresponding steady state found for the two-equation model is unstable, likely a result of over-reduction.

Though not often taught at the K-12 level, declarative programming is a viable paradigm for teaching computer science due to its importance in artificial intelligence and in helping student explore and understand problem spaces. This paper discusses the authors’ design and implementation of a declarative programming course for high school students during a 4-week summer session. The primary goal of the present work is to model disease progression using systems of nonlinear ODEs. The model follows the dynamics of both parasite and immune components. Parasite components considered are larvae, immature worms, mature worms, and eggs. Immune components modeled are resting macrophages, active macrophages and T lymphocytes (T-Cells). We investigate the sensitivity of the model with respect to relevant parameters like rate of granuloma formation, the number of eggs, the proliferation rate of the T-cells, etc. Our findings indicate a saturation in the value of the T-cell population as a function of the rate of granuloma formation. We find that the T-cell population diverges when the ratio of proliferation to death rates exceed a certain threshold value. We then use the Quasi Steady State Approximation (QSSA) to derive two reduced models of schisto-immune dynamics. We compare the behavior of the reduced models to the behavior of the original system. In each case, a linear stability analysis is done. We conclude that the endemic steady states for two of our models are stable, while the corresponding steady state found for the two-equation model is unstable, likely a result of over-reduction.

Cavity flows are very common in everyday life. The undesirable effects of wind moving over an opening manifest itself as loud noise. Examples include noise emanating from the wheel wells of the airplanes during landing or takeoff etc. Likewise, in internal weapons bays and airborne platforms flying at high speed, the flow results in severe vibrations due to resonance and structural failure. The proposed study will investigate the capabilities of numerical algorithms for characterizing the flow field over an open cavity exposed to high-speed flow using computational fluid dynamics (CFD). CFD utilizes the numerical techniques such as finite control volume method, finite difference method, or finite element method to approximate governing equations into forms more suitable for algorithm implementation. The study will encompass fundamental research in the understanding of the numerical solver to treat shock/boundary layer interaction. Currently, two numerical models are being developed. One model utilizes conventional numerical algorithm to simulate the supersonic/high-subsonic cavity flow field. The second model will utilize the high-order shock capturing scheme to solve the governing fluid dynamics equations for modeling the shock/ boundary layer interaction phenomenon. Initial numerical simulations using CFD based on fixed stencil scheme demonstrate that the computed flow field was not depicting the actual features of the flow. Results obtained from the CFD model based on high-order shock capturing show appearance of an expansion fan followed by formation of an oblique shock wave at the base. Work on this project is in progress and results will be presented during the presentation.

Understanding the land use and topology of an excavation site is a necessity for an excavation, because much like farming practices can shatter an urn into pieces, the soil itself is also an archaeological artifact that gets affected by modern-day activity. The BAKOTA project is excavating a Middle Bronze Age cemetery in an area lacking indicators of social stratification typical of the Great Hungarian Plain at this time. Cemetery excavation presents some challenges, however, because multiple landowners and a long and varied history of land use parcel the site into archaeological deposits with differing and varied degrees of disturbance. Oral history provides an important source about land use history for explaining the present soil conditions and helping to inform excavation decisions. This paper consolidates information about known cultivation methods and property ownership using QGIS, providing a visual and spatial reference for further investigation. This undertaking not only provides information to help decide future excavation, but benefits public relations and provides a tool for outreach for the BAKOTA project to inform the present-day residents and stakeholders about the archaeological undertaking in their community.
Evaluating the Effectiveness of Online Computer Science Tutorial Tools in Urban Middle School Students

Andrew Garrett, Kinnis Gosha
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The number of computing jobs is rapidly increasing, unlike the number of qualified individuals to fill these jobs. Diversity has become a big issue in the computing industry and big name tech companies have recognized this and are attempting to address the issue. This research addresses this problem because it will first find the most effective curriculum of two different platforms used to teach fundamental computer science concepts: Google CS First and Koolriculum. The most effective curriculum, of the two, can be used to teach minority scholars (like middle schoolers) computer science, resulting in an increase of minorities pursuing computer science and later obtaining degrees in computer science thus fulfilling the job market's need for computer science graduates.

Which learning platform is more effective in teaching fundamental computer science to middle school students: Google CS First or Koolriculum? The plan is to evaluate the effectiveness of Google CS First and Koolriculum by having three groups (A, B, and C) of students take a computer science pre-test that will be constructed from material in both Google CS First and Koolriculum. Upon completion of both curriculums, results will be gathered by administering a post test to evaluate the performances of all 3 groups. It is hypothesized that group A, who are challenged to complete Google CS First curriculum under the designated amount of time.

Why Fees Signal Performance: An Analysis of ETFs

James M. Gamble IV
Department of Economics, University of Missouri, Columbia, MO

In this study we examine the impact of the emergence of Exchange Traded Funds (ETFs) as alternative investment vehicles to mutual funds. We compare ETF returns, performance and expense ratios to those of mutual funds. We find over time an increased correlation between mutual fund fees and ETF fees and attribute this relationship to increased competition between mutual funds and ETFs. We also find up to a certain threshold actively managed funds are worth their costs.

Data Collection using Mobile Robots

Jiayu He, Praveenkumar Khethavath
LaGuardia Community College, Long Island City, NY

With widespread Wireless Sensor Networks, how to collect data more efficiently became a significant issue in WSNs field. In this research, we will study how to use mobile robot to determine best path and collect data from large-scale environment and sparse wireless sensor networks (WSNs). Each sensor node has its own transmission range limit, integrated robotics and wireless sensors can utilize to solve WSNs problems like range limitation, and relocation or collecting data in hostile environment, etc.

Random walks are used to model diverse phenomena across many fields including physics, chemistry, ecology, and mathematical finance. The classic random walk is a Markovian stochastic process, where the probability of moving forward or backward is homogenous in time. We are exploring exciting random walks (also called cookie random walks), a non-Markovian stochastic process that models motion where past behavior of the walk influences future behavior in that the number of times the walker visited a site determines the transition probability of the next step of the walker. Certain key properties of the walk, such as the recurrence and transience have been explicitly determined as a function of the model parameters. There exists a probabilistic formula for the speed of the walker, but this formula cannot be explicitly computed. We obtained close bounds for the speed of the random walker using branching processes and prove some qualitative properties of the process related to differentiability, concavity, and monotonicity of the speed function.
This project is a study of an efficient parallel implementation procedure of numerical time integration for second-order ordinary differential equations (ODEs) for buildings’ responses to external forces. This multi-processor procedure is implemented using C language and Message Passing Interface (MPI) with parallel data structures and application functions from the Portable, Extensible Toolkit for Scientific Computation (PETSc) library from Argonne National Laboratory.

We establish our desired research results based on the following two steps. In the first step, we implement a prototype parallel procedure to cover a general single buildings’ response model using PETSc time-stepping (TS) routines. As the second step, we extend our implementation to multiple building models for large scale simulations.

This research consists of Pursuit-Evasion in Mobile Robotics which develops algorithms to capture an evading robot in sufficient timing and accuracy. Today there are many instances where an unwanted subject may exist and be dangerous; this research will be able to contribute to the capture of such unwanted subjects and increase safety. By using a robotic simulator, V-REP, and Matlab/Simulink, algorithms are being created to successfully capture an evading robot within a specific environment. V-REP is used to create this environment with obstacles for the robot to avoid. The algorithms created in Matlab will communicate the direction and path for each robot to follow for capture, per environment, and can then be tested for efficiency and success.

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Healthcare using Mobile Cloud Computing is an emergent topic of interest for both industry and research. Healthcare data needs to be secured from unsolicited disclosure when sharing among multiple medical service providers. In this paper, we focus on exchanging healthcare data among doctors and patients’ healthcare service providers. We developed an Android mobile application and a Cloud service to exchange patients’ data among authorized users in a secure and privacy-preserving manner. The Cloud service that we developed performs cryptographic computations, communicates with mobile application and also overcomes the limitations of mobile devices. We evaluate our proposed solution using real-world data sets. The application and also overcomes the limitations of mobile devices.

Unmanned Aviation is a flourishing subset of modern science, and Unmanned Aerial Vehicles (UAV) are the centerpiece of the field. While unmanned vehicles confer a desirable safety benefit, the lack of a human pilot demands sufficient positioning systems. Indeed, unmanned positioning is a critical component of the numerous UAV’s that have been created by the Naval Research Laboratory (NRL). This project involved the creation of the Reconfigurable Aircraft Demonstrator (RAD) STEM Outreach UAV, NRL’s first UAV to be specifically designed for STEM outreach. The RAD project accomplished four goals: design a modular, low-cost STEM outreach platform that would be both a fulfillment of the Navy’s STEM education mission and a captivating promotion of the cutting-edge research being performed at NRL; evaluate various indoor positioning methods for the RAD UAV, make an initial determination of which method is the most desirable based on preliminary evidence, which resulted in the selection of an ultrasonic sensor; and perform quantitative tests on an ultrasonic sensor to determine the feasibility for indoor positioning.

The association between functional connectivity networks and neurological diseases has been established in past studies. Accurately identifying such connections from neuroimaging data, though, is a non-trivial matter, requiring the careful selection of network inference methods, a choice that can be better informed through benchmarking. A systematic comparison of neuroscience network inference methods along with molecular biology and crowd-sourced methods was performed by generating and analyzing in silico fMRI time series based on random and scale-free networks. Results were then evaluated with different statistical metrics. Methods from molecular biology performed well, with GENIE consistently scoring in the top three methods. Creating consensus networks also proved effective, with a consensus of the top five methods consistently outperforming individual methods. A pipeline for inferring brain connectivity networks should include a consensus network of the top five performing methods for improved results.

Poster Presentations

145 Mathematics and Computer Science
Secure and Privacy Preserving Mobile Healthcare Data Exchange using Cloud Service
Doyel Pal, Gobinda Senchury, Praveen Kumar Kethavuth
Department of Mathematics, Engineering and Computer Science Department, LaGuardia Community College, CUNY, NY

146 Mathematics and Computer Science
Accuracy of Ping Ultrasonic Rangefinder for Autonomous UAV Positioning
Isaiah Taylor, Troy Holley, Henry Pickard, Matthew Kelly
Alabama A & M University, Huntsville, AL

147 Mathematics and Computer Science
Pipeline to Infer Functional Connectivity Networks from fMRI Data
Christopher C. Tseng, Shichao Wang, Michael C. Stevens, Reinhard C. Laubenbacher, Paola Vena-Licoca
Center for Quantitative Medicine, UConn Health, Farmington, CT
Emory University, Atlanta, GA
University of Pennsylvania, Philadelphia, PA
Olin Neuropsychiatry Research Center, Institute of Living at Hartford Hospital, Hartford, CT

148 Mathematics and Computer Science
RedStone Shower Mat
Amanda K. Holloman, Seeyed Roosta
Albany State University, Department of Mathematics and Computer Science, Albany, GA

149 Mathematics and Computer Science
Autonomous UAV Positioning
Albany State University, Department of Mathematics and Computer Science, Albany, GA


Studies show that adults 65 years of age and older are more prone to be subjected to bathroom-related injuries and fatalities. According to the Centers for Disease Control and Prevention (CDC), risk factors that contribute towards falling or slipping can be lower body weakness, vitamin D deficiency, various medications, vision problems, and difficulties with walking and balance. Combining these factors increases the chances of one falling despite preventive measures. There are several methods in fall/slip prevention such as shower seats, extra railing and slip resistance mats; however, previous works have failed to not only prevent but also alert in the case of an incident.

We built a pressure sensitive mat can be implemented in homes and establishments. This project will introduce a new way to alert authorities or loved ones’ when the user is in distress and widen the avenue that provides a peace of mind. The Redstone is composed of two parts, hardware and software. We created a prototype using materials from Adafruit wearable’s collection. We use Python programming language to code the software for manipulating stainless thin conductive thread, Velostat pressure-sensitive conductive sheet, and an Arduino Uno are used to create a mat that will record the changes of pressure placed upon it. While the user is bathing, the mat will recognize the constant pressure level being distributed. If there is a sudden change in pressure such as an increase or decrease within five seconds the mat will then record and alert the appointed emergency contact.

Poster Presentations