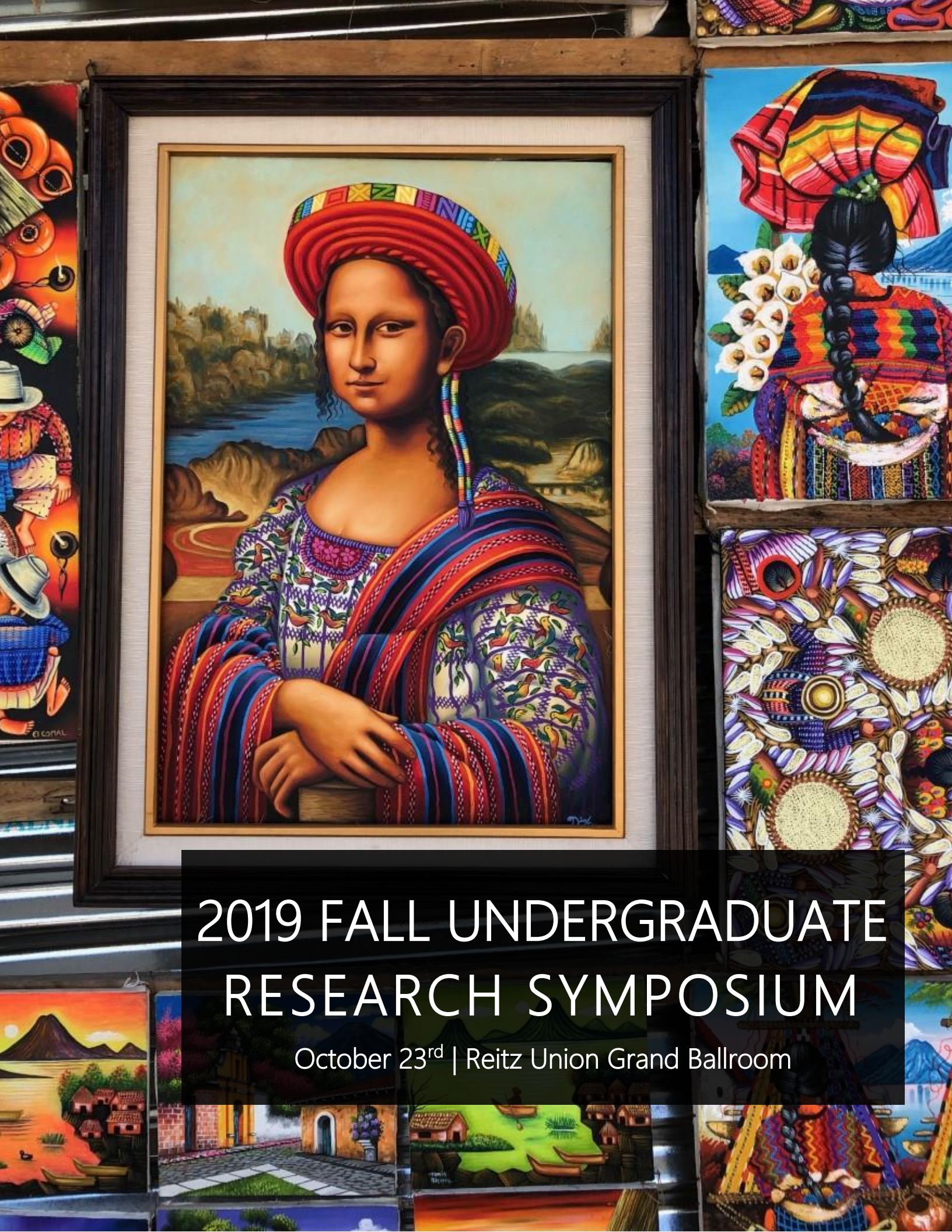
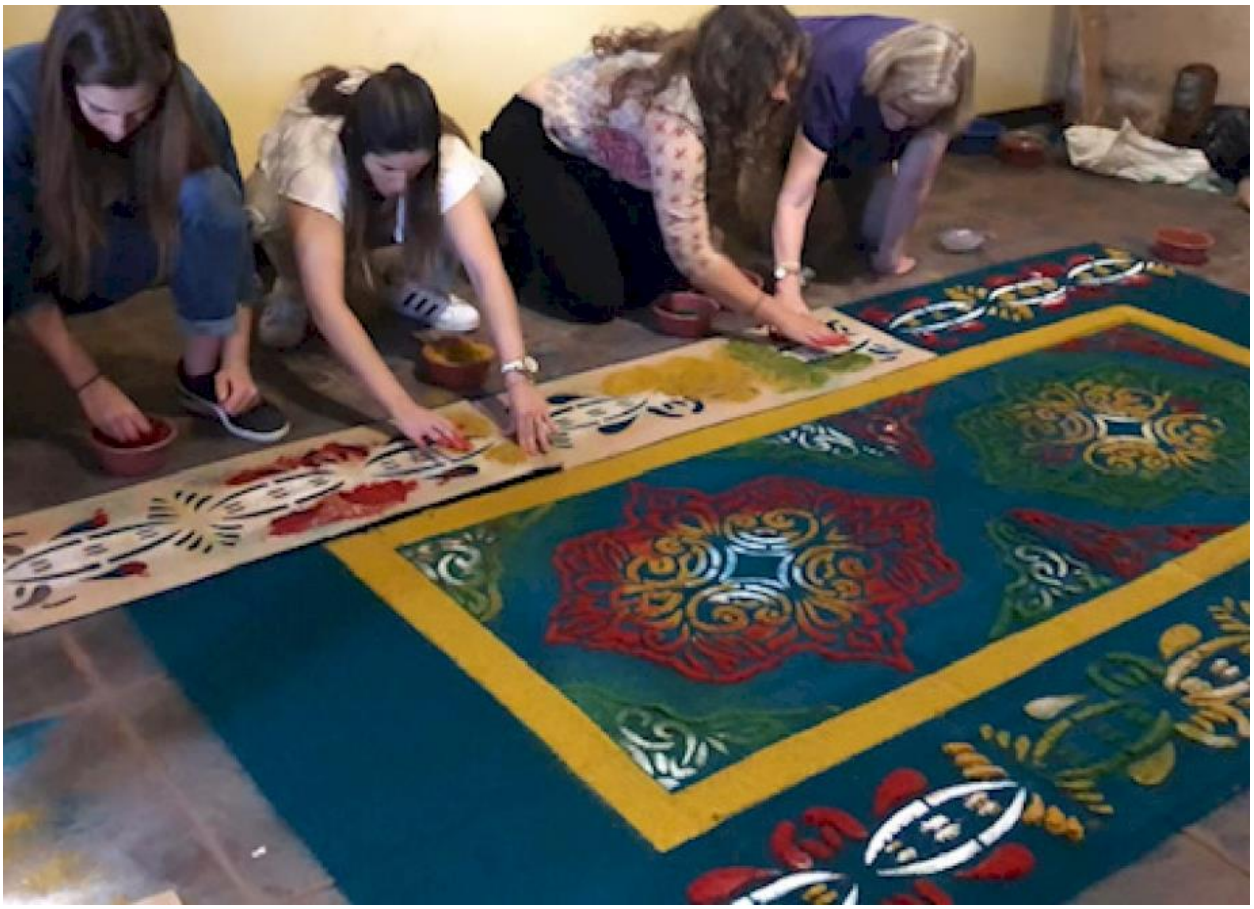


2019 FALL UNDERGRADUATE RESEARCH SYMPOSIUM

October 23rd | Reitz Union Grand Ballroom

Behind the Cover

Antigua, Guatemala (Sacatepéquez)-Dr. Heidi Powell (SAAH) with undergraduate students as part of the Research Tutorial Abroad (UFIC/Center for Latin American Studies) participating in community art making, creating alfombras as part of learning about how arts impact cultural continuity and identity. The students made two alfombras one as an installation in the Museo de las tradiciones de Semana Santa "Sor Juana de Maldondo," a History Museum (below), and one created on March 31st, 2019 as part of a public procession for the procession for El Templo de Santa Ana as a cultural exchange offering to the community on the processional route in the city center.



Students creating the alfombra installation at the *Museo de las tradiciones de Semana Santa "Sor Juana de Maldondo*," left to right, Grace Cope (UG), Amanda Cuello (UG), Liana Zafron (UG), and Carla Pielstick (MA student).

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Trapezius Muscle Model

Alysse Alejandro, Alina Alvarez, Amber Singh

Sculpture

Students often have difficulty understanding the biomechanics of the trapezius muscle, specifically when isolating the three different regions. Through the Arts and Medicine course, the Department of Applied Physiology and Kinesiology at the University of Florida requested a model to be created as a teaching aid. Our trapezius shoulder model was developed through testing multiple iterations. By combining sculpture, mold making, and casting, the final model was formed using plaster, plastic, and silicone. The model allows students to interact with the fibers of the trapezius muscle to mimic the movements seen in the clavicle and scapula. Unlike other models presently known, our model depicts the particular movements of the superior, medial, and inferior fibers of the trapezius, and their interactions with the clavicle and scapula.

Fabrication of a Kinesthetic Anatomy Model of the Subtalar and Talocrural Joints
Cachae Alford, Daniela Lopez, Ashley Somchahmavong, Vidya Narine
Sculpture

As part of the Art, Body, Health class of the College of Art and Art History, our team collaborated with the College of Applied Physiology and Kinesiology at the University of Florida to create a kinetic anatomy model representing the talocrural and subtalar joint movement. Due to the lack of anatomy models that represent both the muscular and skeletal aspects of the lower leg, we decided to create a model of the calf that would exhibit dynamic motion. Our main purpose through this interdisciplinary partnership was to show plantarflexion, dorsiflexion, supination, and pronation through an anatomical model that could aid in the study of motion within anatomy courses.

This anatomy model was accomplished using casting, mold making, and sculpting techniques. We employed materials including sculpting clay (plasticine), plastic, and silicone. The skeletal structure and muscles were sculpted in clay before being molded in silicone or plaster, respectively. After creating such molds, the components of the model were cast in plastic and silicone. At the conclusion of this project, we were able to create a functioning, interactive subtalar and talocrural joint model to facilitate kinesthetic learning for anatomy students.

Exploring the Intersections of Art and Health in Modeling Ankle Movement
Daphne Blessing, Lucia Girado, **Meghan Ta**, Morgan Yacoe
Sculpture

The leg has different combinations of muscles that control the four different movements of the ankle joint: dorsiflexion, plantarflexion, eversion, and inversion. While models of the ankle joint and leg muscles exist in anatomy education, there are currently no existing models that exhibit the muscle actions that cause the different movements of the ankle. Through the Art, Body, and Health course within the College of Art and Art History, we collaborated with the UF Department of Applied Physiology and Kinesiology to create an interactive model that will provide students with an educational tool for better understanding of the muscles responsible for ankle movement. The leg bones were cast out of plastic and silicone and elastic bands were used for flexibility and durability of the muscles. The model is supported by a wooden frame and is able to show the four movements of the ankle by pulling color-coded tabs corresponding to the main eight muscles responsible for its motions. This model allows for interaction and hands-on understanding of the actions and names of the particular muscles. This project was able to utilize the arts in facilitating better understanding of anatomy and the human body.

Interactive and Kinetic Anatomical Model of the Trapezius, Scapula, and Clavicle
Claire Tischuk, Sky Richards, Mimi Diep
Sculpture

Our interactive model of the shoulder demonstrates the upward motion of the scapula and clavicle via the contraction of the trapezius muscle. We were approached by the Department of Applied Physiology and Kinesiology to create a model to aid students in understanding how the inferior fibers of the trapezius interact with the scapula. Students tend to get confused by the upward movement created by the fibers of the trapezius (superior, middle, and inferior) when the inferior fibers appear to have the ability to pull the scapula downward.
To clear this misunderstanding, we created an interactive model allowing students to pull three strings that would contract the corresponding three fibers, moving the scapula and clavicle upwards. Using fabric for the muscles, string for the pulling, plastic for bones, and wood as a supporting base gives our model a unique, abstract impression. We used these materials to be cost effective, demonstrating that models of any price can be useful. We ultimately wanted to give people an understanding of the human body without the hassle of dissection or complex computer programs. This model demonstrates the ease in which art and science can work together and the need that it fulfills.

Geoscience Program Effects on Science Identity and Knowledge in Community College Students

Mingyin Zhu, Kathryn Stofer
Agricultural Education and Communication

As the demand for geoscientists continues to increase, researching the factors to pursuing a geoscience education and career is crucial to understanding how to meet this need. Furthermore, there is a lack of diversity represented in this field. One population that could address this would be two-year community college students, whose demographics tend to be of underrepresented individuals. This study evaluates an extracurricular geoscience program at a two-year community college (2YC) in collaboration with a four-year university. The program includes a geoscience course, science education internship, and research experience over the course of a calendar year. We analyzed quantitative data to understand what students in the study know about geoscience, feel about science and science careers, and feel about their place within the science community. We collected data from program participants using a pre-, post- and long-term post-survey. In individual groups, we have not found significant differences in knowledge, most likely due to the short nature of the course. We will look for factors as to why this is the case. The results of this study will be used to evaluate the effectiveness of this program and to build upon the relatively limited works in extracurricular geoscience programs in 2YCs.

Control of E.coli O157:H7 and Salmonella during production of Ethiopian Qwanta

Gabrielle Allen, Jessica Brown, Morgan McKinney, Alexis Diaz, Sofia Calderon, Bezalem Woldeyohannes, and Jason Scheffler.
Animal Science

Meat provides nutrients that are beneficial for physical and cognitive development, especially in developing countries. When access to meat is limited, and nutrition is poor, safety of food is critical as diarrheal disease are the number two cause of death of children under the age of five worldwide. The objective of this study is to investigate the safety risks associated with traditional Ethiopian dried beef product, quanta. Quanta a whole muscle dried beef product, made using a cutting technique to create elongated, thin strips of meat which are seasoned and air dried. Twenty-gram strips were seasoned with Ethiopian spice Berbere and salt then inoculated with five stereotypes of Salmonella enterica and three strains of E. coli O157:H7. Chambers were created to mimic the air drying process, and ventilation rates were evaluated. Quanta was hung in these chambers for seven days and plated for enumeration 0, 1, 4 and 7d after inoculation. The drying process resulted in a 3.5 0.11 log cfu reduction in E. coli O157:H7 and a 2.7 0.78 log cfu reduction in Salmonella. Air drying without heat treatment does reduce pathogen load, although additional steps should be taken to further mitigate risks.

Effects of Heat Stress on Cellular Processes during Mammary Involution

Valerie Lantigua, Thiago Fabris, Geoffrey Dahl, Jimena Laporta
Animal Science

The health and production of dairy cattle are impacted when cows are heat-stressed during the non-lactating stage coinciding with late gestation (referred to as the dry period, DP). The DP promotes mammary growth, replacing worn-out cells with new cells for milk synthesis. Heat-stress (HS) during the DP suppresses this process, resulting in diminished lactational performance. This research examines the underlying hormonal mechanisms associated with DP HS. We hypothesize that disturbances in prolactin and estrogen concentrations caused by DP HS are responsible for the regulation of mammary cellular processes. Approximately 46 days before calving, cows were enrolled into cooled (n=28) or heat-stressed (n=29) treatments, either cooled with fans and soakers (CL) or uncooled (heat-stressed, HT). Respiration rate, body temperature, and feed intake were measured and mammary gland biopsies (n=7 per treatment) were performed. Tissue explants were divided into three plates and incubated for 24h: a basal media for control, and CL and HT. Media treatments were designed to replicate average concentrations of prolactin and estradiol in CL and HT cows. In future work, this tissue will be used for the gene expression of estrogen-responsive genes and milk-protein genes to evaluate the cellular efficacy of 17β-estradiol and prolactin.

Elevated nitrogen and plant species richness affect milkweed quality and monarch fitness

Rebecca L Perry, **Ava J. Cockey**, Dr. Bryan Unruh, Dr. Jaret C Daniels and Dr. Adam G Dale
Entomology and Nematology

Urban land use is predicted to more than double in the United States by 2060. As urbanization progresses, natural areas are displaced, and insect abundance and diversity typically decline. Golf courses are large green spaces within urban areas common to Florida. Many golf courses are repurposing out-of-play turfgrass areas into conservation habitats. However, research has shown that milkweed exposed to excess nutrients (e.g., fertilizers) can reduce monarch fitness. Since golf courses frequently apply fertilizer to increase turf quality and playability, adjacent monarch conservation habitats may become exposed to increased nutrients. Additionally, plant diversity is known to affect the abundance of insect herbivores that colonize it. Different plant species also occupy different soil niches and utilize resources differently. Therefore, milkweed planted among different species may be affected by nitrogen differently than when planted among only milkweed. In this study, we investigated the effects of high levels of nitrogen on milkweed quality and monarch fitness in monoculture and mixed species plantings. We found that the highest quality milkweed were planted within different species and exposed to high nitrogen. Additionally, higher nitrogen concentrations increased monarch survival to adulthood. Our results are creating evidence-based guidelines to incorporate monarch conservation habitats onto golf courses.

Developing Chironomid Midges as a Model to Study Host-microbe Interactions

Seunghyo Jang, Daniel Perkowski, Xiao Lai, and Adam C.N. Wong
Entomology and Nematology

The influence of microbiome on human growth and development has been recognized in recent years. Laboratory studies have suggested that growth problems associated with malnutrition in early childhood could be mitigated by modifying the gut microbiome, such as through fecal microbiota transplantation. However, the effectors and mechanisms for microbiome-mediated growth promotion are largely undefined. Insects with simple and amenable microbiomes can be used as models to study the role of microbiomes in host growth.

Here, we have set chironomid as a model because of its diverse microbiome and its ubiquitous present in aqua environment and developed a protocol to manipulate the chironomid microbiome. We found that germ-free chironomids took significantly longer time to develop through larval stages and could not survive to adults. An untargeted Liqud Chromatography-Mass spectrometry metabolomic analysis showed there are 17 metabolites that are absent or underrepresented in germ-free chironomids compared with conventional hosts.

Our results suggest that chironomids growth is supported by the microbiome, and possibility through production of specific metabolites. However, the relationships between host and microbe seems very flexible in the context of microbial identity. With this method, we are able to study the host-microbial interaction and identify microbes and metabolites that modulate growth.

Feeding Behavior of Juvenile Leaf-footed Bugs: Attraction to Absent Adults

Kaylin Kleckner, Sara Zlotnik, Christine W. Miller
Agricultural and Life Sciences

Juvenile animals are often less adept at feeding independently compared to their adult counterparts. To obtain critical nutrients, juveniles may use behavioral strategies that make up for morphological limitations, but such strategies are not well understood. We hypothesized that juveniles prefer food sources on which an adult has previously fed because prior feeding damage may make nutrients more accessible. We tested this hypothesis in leaf-footed cactus bugs, *Narnia femorata* (Hemiptera: Coreidae). These insects feed on cactus fruit, but juveniles are less efficient due to their shorter mouthparts. In our behavioral experiments, juvenile *N. femorata* chose between two fruits: one had been fed on by an adult for one week, while the other had experienced no adult contact within the preceding six weeks. As predicted, juvenile insects preferred to stand and feed on the adult-fed fruit over the control fruit. This preference was maintained over a three-day period. Our results suggest that juvenile *N. femorata* maximize nutrient intake by utilizing the feeding holes created by adults or by using adult cues to identify reliable food sources. This study provides insight into behavioral strategies used by juvenile animals to maximize survival in harsh environments.

Optimizing fructose detection in the arbovirus vector mosquito, Aedes albopictus

Sonile Peck, Kara Fikrig, Laura Harrington
Entomology at Cornell University

Aedes albopictus is an invasive mosquito and a disease vector for at least 22 arboviruses. Given its medical importance there is an urgent need to devise new control strategies for this mosquito vector. Toxic sugar baited traps and other strategies hold promise; however, little is known about Ae. albopictus' sugar-feeding behavior in the wild. However, the baseline levels of sugar in non-sugar-fed mosquitoes analyzed with the cold anthrone assay has not been determined, and this could lead to errors in interpreting mosquito sugar-feeding patterns. Furthermore, in field-captured mosquitoes, the presence of fructose from previous blood meals could influence interpretation of the assay. I directly measured fructose content in mosquitoes over a series of days post blood meal ingestion. I found that mosquitoes which ingested blood showed a significantly higher average fructose content when compared to those who ingested only water, and as they digested the blood over the five days, the fructose content gradually decreased over time to undetectable levels. My data creates a baseline for the fructose content of un-fed and blood-fed mosquitoes allowing more accurate estimates of sugar-feeding by field-captured Ae. albopictus. Understanding the sugar-feeding behavior of this invasive species is important for designing new population control interventions.

Preventing Basil Browning: Cloning and RNAi of Polyphenol Oxidase in Sweet Basil
Annelise Vieira, Samantha Burrell, Keun H. Cho, and David A. Clark
Environmental Horticulture

Polyphenol oxidase is a well-characterized enzyme that is largely conserved across plant species and is responsible for catalyzing the rapid polymerization of o-quinones that results in tissue browning. As these oxidation reactions result in significant reductions in food crop commercial viability, nutritional content, and general desirability, regulation of polyphenol oxidase activity presents an opportunity to improve a variety of food crops. Because a basil genome has not been published at this time, the objective of the present work was to determine the gene sequence via molecular cloning for the polyphenol oxidase protein in two commercially-relevant basil varieties, Ocimum basilicum and Ocimum americanum. Following the identification of these sequences, hairpin RNAi constructs were successfully developed for O. basilicum. However, no replicable protocol has been developed to date for the transformation and regeneration of basil in tissue culture and efforts to do so have indicated that basil is recalcitrant in vitro, thus preventing the development of a transgenic basil plant with reduced polyphenol oxidase expression at this time. Future success in developing regeneration protocol for basil may encourage further studies in polyphenol oxidase knock-down using these constructs, as well as quantification of enzyme activity and browning susceptibility in the resultant transgenic plants.

Does Trauma Moderate the Association Between Parent-Child Relationships & Emerging Adulthood Mental Health?

Bailey Bone, Larry Forthun
Agricultural and Life Sciences

This study examined the moderating role of trauma on the association between quality of parental relationships (parental psychological control & parental nurturance) and emerging adult mental well-being (psychological well-being & depression). Self-report measures were completed by 6,442 emerging adults (aged 18 to 29) with a mean age of 20 (SD = 1.99). About seventy-three percent of the participants were female, and twenty-seven percent were male (male n=1735, female n=4707, < 1% missing data). Hierarchical regression analysis and a test for significant interactions using simple slope analysis on low/high trauma (+/- 1 SD) in victim (i.e. abuse, assault, sexual maltreatment, etc.) and non-victim (i.e. accident, illness, injury, etc.) groups was performed. Results showed significant moderation by victim trauma on psychological well-being for parental control. The negative relationship with parental psychological control was only evident with low victim trauma experiences. Depression was also significantly moderated by trauma in terms of parental psychological control. Neither depression nor psychological well-being were significantly moderated by trauma in terms of parental nurturance. Overall, the relationship between parental psychological control and emerging adult mental well-being, in terms of both depression and psychological well-being, was only significant when low levels of traumatic experiences were reported.

Curriculum Development: How Human and Family Services Faculty Envision Student Learning Outcomes

Anna Dreibelbis
Family, Youth, and Community Sciences

The purpose of this study is to evaluate the learning outcomes Human and Family Services faculty deem necessary for their students to learn upon completion of an undergraduate degree program in this field. In addition, this study serves the purpose of evaluating the curriculum review process for a human development and family studies department at a large Southeastern university. The methodology for this study involved hosting three focus groups for faculty members to discuss skills and competencies they consider important for their students. Faculty participated in one of three focus groups, depending on their area of expertise: family science and finances, youth science, and community science/nonprofits. This separation allowed the themes presented in each focus groups to be compared to the other focus groups, and eventually transitioned into the focal point of the student learning outcomes. The results showed 21 themes were similar among multiple focus group discussions. It also allowed for a collective list of 33 student learning outcomes, which will be used by the department's curriculum committee as they complete a curriculum review process.

Self-Care Strategy Utilization Among College Students
Bella R. Polley
Family, Youth and Community Sciences

Self-care is any behavior or attitude in favor of achieving positive mental, emotional, and physical health. This thesis seeks to understand self-care strategy utilization (or lack thereof) among college students. More specifically, this thesis presents self-care strategy information for a sample of University of Florida students as well as a representative national sample of U.S. college students. Following an expert review panel that identified survey items measuring self- care, a secondary data analysis was performed to establish current self-care strategies commonly utilized by college students, as well as changes in these strategies over time. Results indicate that higher education institutions should emphasize preventive self-care methods for students such as life skills and social connectedness. This includes the integration of evidence-based programs on campuses, such as JED Campus, Mental Health First Aid, and Active Minds. Bridging gaps between students and campus resources through effective outreach and programming should also be a priority.
Keywords: self-care strategies, college students, secondary data analysis, resources

Cyberbullying Victimization and Perpetration: A Systematic Literature Review

Victoria Garman, Jordyn McKenzie, **Allison Sickels**
Family, Youth, and Community Sciences

Cyberbullying victimization has been associated with poor academic performance, low self-esteem, depression, and suicidal ideation (Sourander et al., 2010). The National Center for Education Statistics and the Bureau of Justice Statistics (2011) indicate 15% of students experienced bullying online or by text—numbers that turn researchers' attention to identifying possible protective and risk factors. We conducted a systematic literature review to inform implementation of prevention programs that protect youth and families against the negative outcomes associated with cyberbullying. Potential articles (N=4,737) from 4 databases were identified and screened (Academic search premier, PubMed, Web of Science, Compendex); 91 articles were reviewed for eligibility. Final included articles (N=36) met the following criteria: 1) published between 2010-2020, 2) written in English, 3) participants were up to 24 years old, 4) used an intervention design, 5) full-length, peer-reviewed article.These studies found that online environments can traverse all areas of a child's life, impacting the child, school climate, and parental functioning. The literature emphasized using whole-school approaches to prevention programs. Decreasing cyberbullying risk behaviors—moral disengagement, distortion of consequences, and acquisition of blame—were noted along with decreases in homophobic name-calling, sexual harassment, and/or victimization as perceived social conventions increased.

Dentition Photogrammetry for North Pacific Pelagic Sharks

Katherine Boole, Fabio Caltabellota, Zachary Siders, and Robert Ahrens
Fisheries and Aquatic Sciences

Pelagic sharks are an ecologically significant group in the marine environment, especially due to their role as apex predators. While the extent of taxonomic variation within pelagic sharks has been well documented, little is known about the drivers behind their speciation, especially given the high degree of geographic, morphometric, and trophic overlap across taxa. In this study, we aim to use dentition photogrammetry to gain insight on the speciation and niche realization of pelagic sharks in the north Pacific Ocean. We will generate 2D focus-stacked images and 3D wire frame models of teeth from each species in our regional pool using specimens from the Florida Museum of Natural History and other museum collections. These images and models will be analyzed to highlight distinguishing features between species of interest. By pairing these data with an understanding of geographic ranges and ecological roles for each species, we aim to better understand the biodiversity of pelagic sharks and the reasons behind their ability to coexist in a given region. Our results will be made accessible through an open access database to promote further studies into shark trait evolution and the images generated will aid in the current effort to digitize museum collections.

Effects of Trickle and Mass Releases on Humpback Whale Depredation of Hatchery Salmon Fry in Southeast Alaska

Danny Khor, Ellen Chenoweth
Biology at University of Alaska Southeast

Our goal was to determine whether release type of Chinook (Oncorhynchus tshawytscha), chum (O. keta) and coho salmon (O. kisutch) had a significant impact upon salmon survival rates, and whether this impact was affected by the presence of humpback whales (Megaptera novaeangliae) at the time of release. From 2010 to 2015, five release sites in Chatham Strait, Alaska were monitored. Linear regression models were created to explain variability in marine survival for Chinook, chum and coho, with an interaction term included to analyze whether whale presence during fry release had an effect on marine survival. The preferred coho model was the only model that retained the whale presence and release type predictors. For Chinook salmon, marine survival was higher overall when whales were absent during release. For chum salmon, mass releases resulted in higher marine survival rates when whales were absent, while trickle releases resulted in higher marine survival when whales were present. For coho, we saw that trickle releases resulted in higher marine survival rates regardless of whale presence. We recommend that salmon hatchery management takes the fry species and humpback presence into account when selecting a release type to employ.

ZIP14 overexpression in murine pancreatic beta cells leads to diabetes in iron overload

Igor Oliveira, Joseph Olivera, Mitchell Knutson
Food Science and Human Nutrition

Hereditary Hemochromatosis is a genetic disorder characterized by hyperabsorption and accumulation of iron in various body tissues. A common comorbidity in patients with hemochromatosis is diabetes. It is thought that iron accumulating in beta-cells of pancreatic islets leads to damage impairing the production of insulin. Mice do not accumulate iron in islets and do not develop diabetes secondary to iron overload. We hypothesized that an iron loaded mouse overexpressing ZIP14 in beta-cells would develop diabetes. To study this, we generated mice overexpressing ZIP14 in beta-cells (referred as MIP-ZIP14) and bred them with hemojuvelin knockout (Hjv-/-) mice, a model of juvenile hemochromatosis. Histological staining of pancreas tissue sections with Perls' Prussian blue, revealed that Hjv-/-:MIP-ZIP14 mice accumulated iron in beta-cells, while control Hjv-/- mice didn't. Interestingly, male Hjv-/-;MIP-ZIP14 mice develop diabetes by 6-12 weeks of age. Immunohistochemical staining of pancreas for insulin suggests a significant decrease in beta-cell mass in diabetic Hjv-/-;MIP-ZIP14 mice when compared to Hjv-/- littermates. Collectively, our data suggest that we have created a mouse model for the development of diabetes secondary to iron overload. This model will be useful in elucidating how iron loading, specifically in beta cells, leads to their dysfunction.

Effects of Leishmaniasis Infection on Cytoskeletal and Golgi Morphology in Murine Cells

Ileana Acosta, Jeffrey Young, and Dr. Peter Kima
Microbiology and Cell Science

Leishmaniasis, a tropical disease responsible for the deaths of about 65,000 people annually, is caused by an intracellular parasite (genus Leishmania) that is transferred via the bite of a female sandfly. We aim to characterize organelle structure and function of murine cells infected with L. amazonensis. We predicted that infected cells would exhibit altered morphologies in both their cytoskeleton and Golgi apparatus compared to uninfected cells cultured in identical conditions. To investigate these differences, immunofluorescence assays were performed using labels such as anti-GRASP65, DAPI solution and phalloidin staining. The fixed coverslips were observed with an epi-fluorescence microscope and the cells were categorized by infection status and organelle morphology. We found morphological differences in both the cytoskeleton and Golgi of infected cells compared to uninfected cells. This suggests that Leishmania parasites are most likely interacting with their hosts through interactions with proteins from the secretory pathway. Pinpointing these variances in organelle morphology could allow for a better understanding of the effects of infection and can also set the stage for future experiments including drug treatments for Leishmaniasis.

MsrM-type methionine sulfoxide reductase homologous in gram-positive bacteria and hyperthermophilic archaea

Joshua Corbilla, Hasin Sharma, Zachary Adams and Julie A. Maupin-Furlow
Microbiology and Cell Science

Reactive oxygen species (ROS) have been known to cause cellular damage. Methionine is specifically susceptible to ROS by oxidation to methionine sulfoxide. To counteract the damage of oxidative stress, organisms from all domains of life utilize methionine sulfoxide reductase (MSR) enzymes. Recent work reveals a novel type of methionine sulfoxide reductase that uses molybdopterin cofactor for its activity: MsrM (Adams and Maupin-Furlow, unpublished). The overall aim of this project is to better understand this enzyme and its homologs in other organisms, such as hyperthermophilic archaea and gram-positive bacteria (e.g., Bacillus subtilis). Thus far, cloning of the gene that encodes for proteins with Msr activity in two hyperthermophilic archaea and B. subtilis have been performed and all have been tagged with 6x Histidine, as well.

Suppressing the Inflammatory Response in Cancer- SOCS1-KIR
Amari Jones, Jatin Sharma, Joseph Larkin III
Microbiology and Cell Science

An inflammatory response is a natural physiological function in the human body that is essential to fighting infection and foreign molecules in the body. The problem occurs when your body's cells does not turn off this response leading to cell proliferation and subsequent tumor development. A mutation or disruption in the signaling pathway between pro-inflammatory cells can cause them to continue to put out this signal and proliferate. The development of a synthetic peptide, called SOCS1-KIR, has shown the potential to interrupt the signaling of these cells that promote an ongoing inflammatory response. SOCS1-KIR can bind to proteins in the cell and prevent the enzymatic reactions needed to send the cells signal, and in turn, regulates cells responses. We hypothesize that SOCS1-KIR is inhibitory to immune cells such as macrophages that release pro-inflammatory chemicals. Using an MTT Assay, data has shown that SOCS1-KIR is inducing apoptosis in macrophages at the different concentrations of our peptide. At the highest concentration of our peptide we have seen almost a half reduction in macrophages compared to our control of cells that were not treated with SOCS1-KIR. This implies that the peptide is inhibiting cell proliferation and the pro-inflammatory signal.

Isolating ammonia oxidizing archaea through environmental manipulation

Nisreen Shehadeh, Willm Martens-Habbena, PhD.
Microbiology and Cell Science

Ammonia-oxidizing archaea (AOA) play a key role in nitrification, yet their physiological and ecological adaptations remain poorly understood. Understanding their favored environmental conditions is of interest for better understanding of nitrogen cycling in nature and improve nutrient management in agriculture. The objective of this study was to determine the following: which organism is most abundant in an AOA enrichment in a continuous culture bioreactor, which carbon source is preferred, and which inhibitor best isolates the archaeal organism to obtain a pure culture for future analysis. Soil samples taken from the Everglades Agricultural Area were inoculated into enrichment bioreactors and kept in an oligotrophic environment. After a one-year enrichment, PCR and DNA sequencing, and phylogenetic analyses revealed that an archaeon closely related to Nitrosophaera was the most frequent organism. Pyruvate, malic acid, α-ketoglutarate, and a combination of malic acid and α-ketoglutarate were tested as carbon sources. However, none had significant positive effects on its growth based on nitrate, nitrite, and ammonia assays. The unamended control provided the best conditions for archaeal growth. PTIO, ATU, and streptomycin enhanced growth rates of the enrichments. This work suggests an archaeal ammonia-oxidizer is capable of outcompeting comammox bacteria under nutrient limitation without organic carbon requirements.

Evaluating Novel Anti-leishmanial Compounds

Thanh Tran, Jeff Young, Peter Kima
Microbiology and Cell Science

Leishmaniasis is a neglected disease caused by the parasite Leishmania. Leishmania, carried by female sand flies, are spread to a host whenever an infected sand fly takes a blood meal. These parasites then cause multiple clinical manifestations, from cutaneous lesions to deadly visceral infections. Leishmania parasites live within host immune cells to evade detection and elimination. Several drugs are currently used to treat leishmaniasis but there is an emerging resistance plus the drugs can be toxic and expensive. We are focusing on the discovery and development of novel compounds that may effectively treat leishmaniasis through cell disrupting parasite interactions within infected cells. A drug library has been assembled consisting of three parent molecules, Retro-2, Retro-1, ABMA. Previous work has indicated the potential for these compounds to reduce Leishmania infections. Luminescent assays were performed to test the efficacy of these drugs via a strain of L. amazonensis that expresses firefly luciferase; RAW 264.7 cells where infected with this strain. Infections were then treated with compounds of interest and infection burden was assessed by measuring relative luminescence. Preliminary results suggest several compounds efficiently treat leishmaniasis. The drugs showing highest efficacy will be selected for further studies.

Impacts of simulated microgravity on Streptococcus mutans oxidative stress resistance

Cybill Winkel, Matthew Hauserman, Ke Aira Davis, and Kelly C. Rice
Microbiology & Cell Science

Due to several factors, including spaceflight osteopenia, decreased saliva production, and immune dysfunction, astronauts are at an increased risk of dental caries. Streptococcus mutans is a commensal pathogen, contributes to tooth decay, and exhibits altered physiology when cultured under simulated microgravity conditions. To investigate the relationship between host defenses, pathogen virulence factors, and the impacts of microgravity, 50 mL HARVS (High-aspect Rotating Vessel) were inoculated with S. mutans UA159 and incubated while under the effects of two different microgravity models (Rotary Cell Culture System v. Random Positioning Machine) with corresponding normal gravity controls. Samples were retrieved at t = 3 and 6 hours. Each sample was treated with 10mM H2O2; at 30 minute intervals, samples were diluted, plated, and incubated for 48 hours. Cultures grown under simulated microgravity conditions (RCCS and RPM models) exhibited overall lower oxidative stress resistance compared to their normal gravity counterparts. Differences between the two models were noted after conducting the assay using the t = 6 hour sample; S. mutans from both the RCCS model and its control were found to have higher resistance than the RPM and its control. S. mutans' oxidative stress response under simulated microgravity will be further investigated through the generation of knockout mutants.

Chromatin Remodeling in Halophilic Archaea

Emily Winters, **Angelina Nasthas**, Allison Eaton, Paula Mondragon, Ricardo Couto-Rodriguez, and Julie A. Maupin-Furlow
Microbiology and Cell Science; Genetics Institute

Haloferax volcanii, a halophilic archaeon, is known for its ability to thrive in hypersaline environments such as the Dead Sea. Most microorganisms do not tolerate such conditions due to the extreme osmotic stress. Hypersaline environments are often desiccating and exposed to UV which can generate free radicals that damage DNA, RNA, and other important organic molecules. Halophilic archaea have evolved mechanisms to respond to threats generated by the conditions of hypersaline environments. Previous research suggests that oxsR, thought to code for a chromatin remodeling protein, may play a role in the response of halophilic archaea to oxidative stress. We propose that OxsR-mediated alterations to the compact binding of DNA could serve as a mechanism for the defense of halophilic archaea against radicals generated through oxidative stress.

We set out to study the role that OxsR plays in H. volcanii by ligating the gene into a plasmid and adding a C-terminal StrepII tag. The plasmid was then re-introduced to an ΔoxsR mutant strain. The addition of the C-terminal strep II tag may allow for purification of the protein by StrepII affinity chromatography. Once OxsR is purified, we will analyze its binding and remodeling of genomic DNA in vitro.

West Indian Marsh Grass Seed Viability in Varying Conditions

Sara Humphrey, Candice Prince, Stephen Enloe
UF/IFAS Center for Aquatic and Invasive Plants

The invasive West Indian Marsh Grass (WIMG), fundamentally changes wetland ecosystems in Florida. WIMG primarily disperses via seeds, but little is known about viability or seedbank conditions that may affect germination. This research evaluated the effects of storage conditions on WIMG germination in growth chambers, and the effects of hydrology on germination in a greenhouse. Seeds collected in 2015 and 2017 were stored in either wet or dry conditions until April 2019. They were soaked overnight in water or KNO3, placed in a germination chamber, and assessed for germination every three days for over 3 weeks. Seeds from 2018 were established in a greenhouse under four different hydrologic regimes (dry, drained, saturated, and inundated), and assessed for germination over 30 days. Results from the growth chamber study suggest that dry seeds remain viable for at least 4 years, where seeds under flooded conditions are not likely to germinate after 2 years. Further, the germination disparity between H2O- and KNO3-treated seeds indicates that WIMG seeds have some level of dormancy. The results of the 2018 study support those from the growth chambers, suggesting that flooding suppresses WIMG germination.

Do Parasites Infect Optimally?

Rayann Dorleans, Theresa Jones, Ashwini Ramesh, Farrah Bashey-Visser
Wildlife Ecology and Conservation

Optimality theory states that organisms will behave in ways that are the most beneficial to their survival. This is visible in larger animal such as various livestock which feed, mate, and reproduce in groups of various sizes according to their needs. Less is known about how optimality theory applies in a host parasite relationship. In order to explore this, we used a nematode-caterpillar model. We infected several caterpillars with varying densities of nematodes. So a group of caterpillars were infected with 20 nematodes, another with 50, and so on. We then measured the effects on fitness based on the size of female nematodes that resulted from each infection dose with every density tested being repeated with two different nematode strains. We then compared the number of nematodes that successfully infected to the female size. To observe if parasites follow optimality conditions, we created several mesocosms each with varying nematode densities and placed caterpillars within them, allowing them to infect naturally. This was done in order to test if the nematodes actually displayed the behavior we observed in the lab in a natural setting.

A Specific Farnesyl Diphosphate Synthase Controls the Production of Anti-Fungal Zealexins in Maize

Drake Rose, Hoang Tang, and Anna K. Block
United States Department of Agriculture (USDA)

Zea mays (maize) produces sesquiterpenoid defense compounds called zealexins in response to fungal infection. These compounds exhibit antimicrobial activity, with their accumulation at the site of infection likely inhibiting fungal growth. Farnesyl pyrophosphate (FPP), a fifteen-carbon precursor to such compounds, is produced by farnesyl diphosphate synthases (FPPS)—enzymes encoded by three genes in maize (fpps1, fpps2, and fpps3.) In order to investigate if a specific fpps gene controls the production of zealexins in maize, we examined their expression in response to fungal infection and created CRISPR/Cas9 derived loss-of-function mutants in each of the genes. Measurement of zealexin production in stems of plants infected with the fungal pathogen Fusarium graminearum showed that fpps3 mutants accumulated significantly reduced levels of zealexins compared to wild type plants. These data indicate that fpps3 controls defense related production of FPP.

House Beautiful Magazine's Climate Control Project: Climatic Design and Regionalism in Postwar America

Carolyn Muldowney and Vandana Baweja
Architecture

Postwar suburban development was facilitated by the availability of cheap fossil fuels coupled with the rising use of mechanical conditioning systems, especially air-conditioning. Consequently, as the 1950s progressed American postwar builders chose to build houses in cookie cutter suburbia without any regard for building in accordance with the local climate. A popular design magazine House Beautiful launched the Climate Control Project (1949–1952). The Climate Control Project was an attempt to educate builders and architects on how to build sympathetically with the climate so that energy bills could be lowered through simple technologies such as orientation, shading, protection of windows, and planimetric arrangements. Elizabeth Gordon (1906–2000), the editor of House Beautiful from 1941 to 1964, championed the Climate Control Project. This study will explore how House Beautiful created the idea of a regional postwar home using climatic design. House Beautiful published climatic data for different regions in the United States that comprised mean temperatures, wind speed and direction, and precipitation and humidity levels. The magazine then published design guidelines for how best to build in that climate through design techniques such as – orientation; site planning; roof design; window design; spatial planning of the interior; and using the best possible materials.

Urban Development and Waste Management in Verón, Dominican Republic

Leah Locascio, **Elijah Crain**, Carlos Perez Ferrer, Hugh Dennin, Ewa Wiercioch, Tim Murtha
Landscape Architecture and Florida Institute for Built Environment Resilience (FIBER)

Our research was designed to document and quantify the waste management activities in the rapidly urbanizing settlements of Verón, Dominican Republic. Changing daily, Verón is home to a mix of older, informal, densely settled, and rural communities, and newer, more formally planned and constructed communities, all, established to meet the growing labor demand for tourism in Punta Cana. We first documented infrastructure using the Open Street Map Platform. This data provided a baseline for field observations and UAV survey. We surveyed six residential communities and systematically applied pedestrian surveys to quantify and qualify the types and amounts of waste present. Using this data with UAV maps, we produced a comprehensive visual of waste distribution for each community. These data allowed us to investigate relationships between types and amounts of waste and the physical form of the neighborhoods. For example, some highly dense neighborhoods had waste bins and systems that were successful at managing waste. Other, less dense settlements had fewer bins and less controlled waste disposal. While this was a preliminary study focused on research design and field observations, it offers an important window into the challenges facing rapid urbanization and the expansion of tourism in the Caribbean.

Evoking Regenerative Properties of Adipose-derived Stem Cells Using Electrical Stimulation

Raffae Ahmad, Nora Hlavac, Deanna Bousalis, Christine Schmidt
Biomedical Engineering

Electrical stimulation has been shown to induce regenerative processes in tissues and has been utilized in the creation of bone growth stimulators and wound healing devices. One promising therapeutic avenue is to use electrical stimulation for the purpose of priming stem cell behavior to be reparative and pro- regenerative. In particular, electrical stimulation of cultured adipose-derived stem cells (ASCs) to produce regenerative factors may be a promising strategy for treating injury as they can be readily sourced. This study aimed to define patterns of ASC behavior following varied electrical stimulation regimes as a function of their expression of pro-regenerative factors for wound healing and neural injuries. Electrical field strength, pulse frequency, and time of stimulation were specifically varied to determine what effects these properties have on ASC behavior. Significant changes in ASC gene expression of factors such as vascular endothelial growth factor and brain derived neurotrophic factor were demonstrated following stimulation. These results indicate a promising strategy for modulating expression of pro-regenerative factors in vitro for use in therapeutic applications. Future work will evaluate if trends in increased gene expression are translated to proteins produced by ASCs. Furthermore, electrical stimulation parameters will be further optimized to harness regenerative ASC properties.

Characterization of Dexamethasone-Loaded Silicone for Local Drug Delivery

Brandon S. Badamtchian, Kaitlynn P. Olczak, Kevin J. Otto
Biomedical Engineering

This work characterizes dexamethasone-loaded silicone to determine the ability of silicone insulation to be utilized for local dexamethasone (dex) delivery. Silicone was loaded with dexamethasone 21-phosphate disodium salt. Wires were dipped in the silicone solution 4 or 8 times, and cured for 1 hour at 100°C. Wires were imaged and measured with electrochemical impedance spectroscopy (EIS) then stored in PBS to measure drug release, EIS, and swelling over 7 days. Drug release was calculated from spectrophotometer measurements. Swelling was measured by taking images of the wires and measuring changes in thickness with ImageJ. For EIS, the measured open cell potential (OCP) was used as the "pseudo-zero" for the 20 mVp-p sinusoidal perturbation. The frequency was swept logarithmically from 100 kHz to 50 mHz, and 35 measurements were taken between these frequencies. After 7 days there was no significant difference in thickness change between coatings with or without dex ($p > 0.05$). The entirety of dex is not released in a 7-day timeframe. There was no significant change in impedance differences between the dex and no-dex samples at 10 kHz and 1.3 kHz after 7 days ($p > 0.05$). Silicone insulation is therefore a suitable method for local dex delivery.

Optimizing Site-specific Galectin-1 Cross-linking via Poly(ethylene glycol)

Bryant Kane, Margaret M. Fettis, Gregory A. Hudalla
Biomedical Engineering

Galectin-1 (Gal1) is an immunomodulatory protein that has demonstrated therapeutic potential for treatment of autoimmune conditions in various pre-clinical models. However, translation of Gal1 is hindered by two unique biochemical features. First, Gal1 has 6 cysteine residues, 4 of which reside on the surface, which can cause inactivation of the protein in oxidative conditions. Second, the active conformation of Gal1 is a non-covalent homodimer with a high dissociation constant (KD = microM). 3 of 4 surface cysteines (C2, C16, and C88) can be mutated to serine without loss of activity. Further, the remaining cysteine (C130) can be used to site-specifically crosslink Gal1 into a stable homodimer via reaction with poly(ethylene glycol) PEG diacrylate; Gal1-PEG-Gal1 is active at concentrations an order of magnitude lower than un-"pegylated" Gal1. We chose C130 as the initial pegylation site because it is the closest to the native dimerization domain. Data will be presented characterizing the crosslinking of Gal1 into a stable homodimer at all surface cysteines, as well as the comparison of crosslinking via PEG dimaleimide (PEGMal) versus PEG diacrylate (PEGDA).

Bioprinting Stem Cell-Derived Cardiac and Cortical Cultures to Engineer Complex in Vitro Tissues

Elisa Nieves, Martin Tomov Ph.D., Samantha Lanjewar, Steven Sloan MD Ph.D., Vahid Serpooshan Ph.D.
Biomedical Engineering

Bioprinting has emerged as an extension of conventional 3D printing and additive manufacturing techniques, enabling creation of functional 3D tissues and organs. It enables researchers to fabricate intricate, precise structures that are highly reproducible. One major challenge in tissue bioprinting is the harsh environment that cells often endure during the printing processes. This can include changes to pH, temperature, nutrients, pressure, and shear stress. These environmental factors, together with the restricted cell-to-cell interactions in printed tissues, have limited the success of bioprinting certain cell types including cardiomyocytes and cortical neurons. To combat these issues, here we examine 3D bioprinting of stem cell-derived embryoid bodies (EBs) which allow for effective intercellular connectivity and can fuse with neighboring spheroids to create even larger constructs. We encapsulated human induced pluripotent stem cell-derived EBs within a 10% gelatin methacrylate (gelMA) bioink and printed linear constructs using a BioX printer. Optimal crosslinking of bioprinted lines to retain cell viability was obtained using UV at 6 mW/cm2 for 30 secs. Printed constructs survived for > 30 days in vitro culture and are currently being differentiated into cortical neurons.

Assessing the Capacity of a Novel Human Placenta-derived Matrix in Inducing Angiogenesis and Osteogenesis

Sydney Shriver, Mediha Gurel, Eman Shreteh, Calum McFetridge, and Peter McFetridge
Biomedical Engineering

Translating successful laboratory results from in vitro and in vivo studies into a clinical setting is a significant challenge faced by the regenerative medicine community. A specific example would be in revascularizing traumatic tissue injuries in order to reestablish nutrient and waste exchange. A novel approach to combat these challenges is using a growth factor rich human-based extracellular matrix that is derived from healthy placentas - human placental matrix (hPM). hPM is an immunologically privileged tissue, hypothesized to enhance angio-inductive and osteo-inductive capacities. When seeded onto hPM coated wells, Human Umbilical Vein Endothelial Cells (HUVECs) and Human Mesenchymal Stem Cells (hMSC) demonstrated morphology characteristic of angiogenic formation. As well, hMSC predifferentiated toward an osteoblast phenotype displayed significantly higher calcium deposition in both conditions containing hPM when compared to the control condition cultured in basal growth media (BGM). These results suggest that hPM induces vasculogenesis and osteogenesis in vitro. These results also show that hPM and hMSC together may provide a favorable environment for the development of novel therapeutic alternatives and multilineage differentiation. Overall, this serves as a valuable introductory study into the potential for hMSC and hPM to be used in vivo for such applications.

Engineering Superior VEGF Antagonists

Leilani Astrab, Angela Zhu, Patrick Krohl, Rakeeb Kureshi, and Jamie Spangler
Biomedical Engineering at Johns Hopkins University

Ocular neovascularization drives pathogenesis of diseases like age-related macular degeneration and diabetic retinopathy, two leading causes of blindness in adults. Vascular endothelial growth factor (VEGF) is a protein that serves as a stimulus of neovascularization; blocking VEGF activation of its receptor (VEGFR) has shown benefit in treatment of retinal eye diseases. The FDA-approved drug aflibercept is a VEGFR mutant that acts as a decoy receptor to prevent VEGF engagement of VEGFR and consequent signaling. Aflibercept provides a basis for VEGF-neutralizing therapies but has limitations that leave room for further improvement. The drug has an affinity for VEGF similar to native receptors, hindering antagonistic activity, and only targets one type of VEGF, leading to drug resistance. This project aims to address these limitations by increasing drug affinity for VEGF-A and evolving cross-reactivity with VEGF-C to prevent resistance. We designed a mutagenic library of aflibercept to identify high-affinity clones that could act as superior therapeutics in treating retinal eye diseases. Clones were characterized using bio-layer interferometry, cell surface competition assays, and rat models of macular degeneration. Studies of the clones' characteristics compared to aflibercept suggest that the clones have superior anti-angiogenic properties and could therefore serve as exceptional VEGF antagonists.

Developing Natural Based Thermally Gelling Bio-inks for 3D Tissue Engineering

Kata Alilovic, Jorge A. Mojica Santiago, Christine E. Schmidt
Biomeical Engineering

Hydrogels based on extracellular matrix (ECM) components are widely used as bio-inks to mimic native tissues. Collagen is the most abundant ECM component found in different types of tissues, while laminin, hyaluronic acid, and fibrin are important to maintain ECM physiology. Gelation of collagen occurs at physiologically relevant temperatures which makes its pre-hydrogel solution thermally sensitive. Since maintaining ideal culture temperatures is vital for optimal cell proliferation, this study focuses on the rheological characterization of thermally gelling natural materials and combining them as a potential natural bio-ink for extrusion-based 3D printing. To characterize temperature-dependent rheological properties of the pre-gel solutions and determining gelation point, a temperature ramp between 4 °C and 37°C was conducted at rates of 5°C/min and 35°C/min. Once the temperature reached 37°C, measurements were taken for 30 minutes. Complex viscosity, storage modulus (G') and loss modulus (G'') were measured as a function of time for all materials. The gelation point was calculated from the rheometer. All pre-gels showed an increase in G′ and G′′ over time as temperature increased to a steady-state, indicating when they reached gelation. The same trend was recorded for complex viscosities of pre-gel solutions.

Calibrating Center-to-Center Distance Between 3D Printable Heterogeneous Hydrogels to Increase Geometric Fidelity in Calcific Aortic Valve Disease

Maximillian Rozenblum, Benjamin Albert, Jonathan Butcher
Meinig College of Biomedical Engineering at Cornell University

Aortic valves presenting calcific aortic valve disease (CAVD), one of the leading valve-related diseases, experience diminished valve function. Patients with CAVD are often considered candidates for transcatheter aortic valve replacement (TAVR) to restore blood flow. However, calcific nodules may interfere with expansion of the TAVR stent, leading to blood leaking around the replacement valve. Modifications to the TAVR procedure include integration of biological substances and modeling CAVD in a finite element analysis (FEA). Ultimately, both are ineffective as cross talk between involved cell lineages is not completely understood and FEA models fail to account for cardiac morphological variation. A tool that may allow for pre-procedural prediction of TAVR success is 3D printing of patient-specific valve geometry and biomimetic mechanical properties. We printed hydrogel groups onto a glass slide and characterized the fusion between layers in an attempt to minimize overlap of layers printed too close together. Each slide was imaged, thresholded, and binarized in MATLAB. Ideal overlap was achieved when the height of a singular extrusion matched that of two fused extrudants. Characterization of hydrogel compositions could provide researchers a protocol to explore different hydrogel compositions, or physicians insight into predicting individual patient outcomes of a TAVR procedure.

Exploring the use of silk fibroin from Plodia interpunctella for applications in tissue engineering

Ali H. Lateef, Richard B. Furlong, Paul D. Shirk, Whitney L. Stoppel
Chemical Engineering

Silk fibroin from Bombyx mori silkworms has been widely studied for tissue engineering applications, exploring the properties silk materials. Silk fibroins produced by other moths have not been explored to the same extent. Thus, we aim to explore the properties of silk fibroin produced by the Indianmeal moth (Plodia interpunctella) (IMM). The current project is part of a joint effort with the overall objective to study the silk-producing order Lepidoptera. We hypothesize that silk from other Lepidoptera families may have properties that can be employed for use as a biomaterial in tissue engineering. To purify and regenerate the silk fibroin from the IMM, protocols designed for fibroin from B. mori will be adapted. Changes to already written protocol includes scaling down the process, varying the boiling time and the concentration of the lithium bromide used for solubilizing the silk fibroin protein. Lastly, mechanical testing the IMM biomaterials will be subjected to atomic force microscopy and shear and uniaxial rheology to assess the elastic properties of the IMM fibroin as well as quantify the variability of the silk produced by the moths. In conclusion, we are working to quantify the different properties of the silk produced by Indianmeal moths.

Green Conversion of Glycerol To Lactic Acid

Daniel Aziz, Giada Innocenti, Carsten Sievers
Chemical Engineering at Georgia Institute of Technolog

There has been a growing need to replace the world's dependence on fossil fuels. Biofuels offer an immediate and efficient solution. To increase the economic viability of a biodiesel production, the abundant side product of Glycerol (1 gal glycerol: 10 gal biodiesel) must be upgraded to a more valuable chemical such as Lactic Acid which has key applications in the synthesis of biodegradable plastics. To accomplish this conversion, a continuous liquid flow packed bed reactor was built in an industrially scalable fashion. Au-TiO2 catalyst was used due to its favorable acidic and basic properties. NaOH and molecular Oxygen were used as sources of Oxygen to enable the conversion. Reaction products were analyzed by High Performance Liquid Chromatography. The separation method was optimized at 3µL injection volume, 30°C, and 0.4ml/min flow rate. Reaction conditions of temperature, flow rate, oxygen concentration, and catalyst presence were varied. The conversion was found to be heavily dependent on oxygen concentration.

Challenges facing electrospun scaffolds for small diameter vascular tissue applications

Zion Iverson, Josephine Allen
Materials Science and Engineering

Cardiovascular disease is the leading cause of death worldwide. Complications caused by this disease, such as atherosclerosis, lead to arteriole damage often causing vascular tissue to be replaced through surgical intervention. Electrospinning offers a cost-effective method for producing for cheap, readily available vascular grafts. Unfortunately, the alignment of the uniform fibers produced by electrospinning often decreases the porosity of the scaffold preventing cells from infiltrating into dense, 3D scaffolds. In addition to porosity, the current methods for crosslinking scaffolds involve toxic glutaraldehyde (GTA) vapors. Biodegradable scaffolds crosslinked using GTA vapors risk immune response as free aldehydes are released during degradation. This work focuses developing a method for introducing polyvinyl alcohol (PVA) microparticles into fibrous gelatin and polycaprolactone scaffolds to increase porosity. Alternative crosslinking methods using the natural aldehydes cinnamaldehyde and vanillin are investigated to bypass glutaraldehyde toxicity. This work is a promising step towards increasing cellular infiltration and proliferation, and providing non-toxic methods for crosslinking in dense, 3D vascular tissue scaffolds.

NEAMS Workbench Applications: Modeling Metallic Fuel in Bison for Versatile Test Reactor (VTR) Development

Kaylee Cunningham, Robert Lefebvre, Jeffrey Powers
Nuclear Engineering at Oak Ridge National Laboratory

Summer 2019, UF Nuclear Engineering student Kaylee Cunningham worked with Oak Ridge National Laboratory (ORNL) mentors Jeffrey Powers and Robert Lefebvre to benchmark the Bison nuclear fuel performance analysis tool, developed by Idaho National Laboratory, by modelling ternary metallic fuel as part of an effort to advance the Versatile Test Reactor (VTR) project. Bison was used through the Nuclear Energy Advanced Modeling and Simulation (NEAMS) Workbench program, which enabled smoothly integrated workflow operations that included the streamlining of creating, reviewing, executing, and visualizing integrated modelling and simulation tools. Specifically, modelling aUranium-19%Plutonium-10%Zirconium (U-19Pu-10Zr) pin from the 1985 Integral Fast Reactor (IFR-1) irradiation experiment at the Fast Flux Test Facility (FFTF) produced burnup results within 5% relative error of the actual experiment, temperature values roughly 25 Kelvin off, and demonstrated gap closure slightly late. Given the relatively small margin of error, the results were determined to be generally successful though some future model improvements were identified. Likewise, through this work, NEAMS Workbench workflow was enabled across operating systems and job launch on computing resources was streamlined. Currently, the student continues research with her ORNL mentors with a focus on improving and simplifying the usability of Bison through the NEAMS Workbench platform.

Defining an Orthogonal Type System for Mutability

William Anderson
Independent Research

Programming languages can restrict the mutability of individual objects to provide certain guarantees to developers. This paper explores an orthogonal type system which identifies five levels of mutability and the resulting properties. These levels are readable, mutable, unique, immutable, and constant; each of which provide their own restrictions for what can safely be done with a particular object or reference. By treating mutability as being distinct from the class, an individual type can support different levels of mutability without the need for separate subtypes and is completely independent (hence, the system is orthogonal).

The knowledge of mutability provides many useful guarantees to developers. Immutable objects can be safely shared, even across threads. Constant objects can be compile-time constants and may be used as map keys. Readable references allow for objects to be shared without needing defensive copies. Lastly, unique references may be converted to immutable variants or completely transferred between programs. As a result, compilers may make optimizations that were previously impossible to do safely in order to improve performance. Additionally, developers can now establish more specific contracts in their programs to reduce issues while retaining all of the benefits of mutable state.

Attention Training on Smartphones (ATS): The Beginning

Patricia Chauca, Tessa Frohe, and Robert Leeman
Health Education and Behavior

The opioid epidemic has affected millions worldwide and continues to increase. Pain often initiates and sustains frequent opioid use, so understanding opioid use and associated risks is especially important for overdose prevention. Attentional bias (AB) occurs when someone pays inordinate attention to substance-related cues. AB has been related to a higher likelihood of relapse. Attentional bias retraining (ABR) has shown promising results in reducing AB to substance cues with alcohol and cigarette users, but there has been little research among opioids users. Distributing ABR through mobile devices as an application is inexpensive, convenient, and can be widely distributed. In the Attention Training on Smartphones (ATS) study, we are testing the effects of ABR via smartphones with patients, ages 18 – 50, currently receiving treatment with buprenorphine, Suboxone or methadone for an opioid use disorder (OUD). ABR will be distributed through an app in the participant's natural environment. This summer I worked on creating, editing, and testing assessment tools such as intricate surveys, study instructions, and app testing. I have also assisted with recruiting and screening participants for eligibility through the phone and in-person screening appointments, which gives us a more in-depth view of patients' OUD and pain.

Measuring Sexual Risk-Taking: A Systematic Review of the Sexual Delay Discounting Task

Meher Kalkat, Neo M. Gebru, Maggie Ansell, Meredith Berry, Robert F. Leeman
Health Education and Behavior

The Sexual Delay Discounting Task (SDDT; Johnson & Bruner, 2012) is a laboratory task capturing sexual risk-taking, measuring overall likelihood of condom use and willingness to wait for sex when condom availability is delayed. The SDDT has high ecological validity as a model of actual sexual risk-taking. The task can also be used to test effects of substance administration on sexual risk-taking behavior. The SDDT has been utilized in several studies, but there remains a lack of standardization in task administration, data analysis, and reporting across studies using the SDDT, reducing the generalizability of results. We conducted a systematic review comparing use of the SDDT across studies to assess discrepancies in its implementation and implications for understanding associated results. This study utilized Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology, yielding 17 peer-reviewed articles. Initial results indicate differences in the implementation and data analysis of the SDDT, including lack of uniform criteria to determine outliers; lack of standardized protocol for selection of photograph stimuli used in the task; and differences in time intervals posited to participants in the task. This information has implications for exploring relationships between sex-related delay discounting and clinical problems that impact public health.

Neighborhood Characteristics and its Association with Problematic Cannabis Use in Truant Adolescents

Daniel Moolchand, Ricarda Pritschmann, and Ali Yurasek
Health Education and Behavior

Recent research demonstrates an increase in cannabis use among adolescents. These increased prevalence rates coupled with the negative consequences associated with early cannabis use, highlights the need for more research examining risk factors and predictors of use in this population. Behavioral economic theory suggests that contextual factors such as socioeconomic status, neighborhood characteristics, and the availability of non-substance involved activities are related to substance use in adolescents. Despite this relationship, little work has looked at these variables in truant youth. Hence, the purpose of this study is to examine the relationship between environmental factors (including recreational facilities, neighborhood surroundings, and crime) and problematic cannabis use in approximately 100 cannabis using, truant adolescents. This study will utilize data from an ongoing project examining behavioral economic variables and substance use among truant youth. Pearson's correlations will be used to examine the associations between the proposed variables. Findings from this study can be used to identify potentially modifiable targets for intervention and prevention programs.

Ketamine Science for Mental Health: A Cognitive Map Analysis of Expert Communication

Rocio Alberto, Elizabeth Barbour, Naomi D. Parker, Yulia A. Strekalova
Mass Communication

Mood disorders and chronic pain affect millions of people today and can have debilitating symptoms, causing victims to struggle throughout their daily lives. Consequently, researchers and medical professionals are always searching for ways to treat these disorders. In our research, we examine Ketamine as a treatment for mood disorders and chronic pain and how providers present information about this treatment to patients and how patients discuss benefits of Ketamine therapy.

This mixed-methods study employs cognitive map analysis (CMA) to identify causal beliefs presented in expert communication. First established in 1970s (Axelrod, 1976), CMA focuses on cognitive structures articulated in speech or text. It uses systematic textual analysis to identify causal relationships and interconnections among them. Following the first, qualitative stage of the analysis relationships are assessed quantitatively using matrix agenda and network analysis (Kosko, 1986). CMA has theoretical implications for the understanding of expert and lay cognitive structures and decisional pathways. The results of CMA analysis can also be used for message design and decisional outcome modeling.

Most expert communication suggests a negative relationship between Ketamine and chronic symptoms. For example, ketamine is said to treat antidepressant resistant depression by increasing the synaptic connections between nerve cells in the brain.

Cognitive Map Analysis of Expert Communication about Pain Management in Cancer

Nabiha Azaz, Hansberry Pierre, Naomi D. Parker, Yulia A. Strekalova
Mass Communication

This research project analyzed messages about pain management by NCI-designated cancer centers. Our goal was to assess causal relationships presented on these webpages. This mixed-methods study employs cognitive map analysis (CMA) to identify causal beliefs presented in expert communication. First established in 1970s (Axelrod, 1976), CMA focuses on cognitive structures articulated in speech or text. It uses systematic textual analysis to identify causal relationships and interconnections. The qualitative stage of the analysis relationships are assessed quantitatively using matrix agenda and network analysis (Kosko, 1986). CMA has theoretical implications for the understanding of expert and lay cognitive structures and decisional pathways. The results of CMA analysis can also be used for message design and decisional outcome modeling. Our preliminary analyses show that messages focus on similar holistic treatment plans. Not many centers go in depth about specific prescriptions. One causal relationship that discussed opioids found that "opioid treatment can improve the lives of people with cancer" (Sparks, 2018). While opioids were promoted as a means to reduce treatment pain, warnings were also issued about their potentially harmful side-effects. Analyzing how cancer centers discuss the benefits and risks of pain medications has implications for developing more effective patient education materials.

Expert Communication about Juicing and Cancer: Cognitive Map Analysis
Rodaina M Elsayed, **Shamika Louis**, Naomi D. Parker, Yulia A. Strekalova
Mass Communication

Juicing is one method for cancer patients seeking to improve their health through diet. This study analyzes how information about juicing is presented to cancer patients on the websites of NCI-designated cancer centers. First established in the 1970s (Axelrod, 1976), CMA focuses on cognitive structures articulated in speech or text. It uses systematic textual analysis to identify causal relationships and interconnections among them. Following the first, qualitative stage of the analysis relationships are assessed quantitatively using matrix agenda and network analysis (Kosko, 1986). CMA has theoretical implications for the understanding of expert and lay cognitive structures and decisional pathways. The results of CMA analysis can also be used for message design and decisional outcome modeling. The findings from this study indicated that the websites highlighted nutritional benefits of juicing such as increased immune system function and improving digestion. These benefits were presented as helping to fight cancer, but not to cure it. Many experts on the websites also noted that juicing should be used as a supplement to boost health, rather than be the patient's main source of diet or cancer treatment.

Expert Communication about Depression and Cancer: Cognitive Map Analysis

Gloria Montoya-Vazquez, Naomi D. Parker, Yulia A. Strekalova
Mass Communication

Receiving a cancer diagnosis has several impacts on a patient's well-being and emotional health. In order to find how NCI- designated cancer centers across the country are addressing the impacts, including depression and how it relates to the patient, we analyzed depression specific pages of their websites. This mixed-methods study employs cognitive map analysis (CMA) to identify causal beliefs presented in expert communication. First established in the 1970s (Axelrod, 1976), CMA focuses on cognitive structures articulated in speech or text. It uses systematic textual analysis to identify causal relationships and interconnections among them. The qualitative stage of the analysis relationships is assessed quantitatively using matrix agenda and network analysis (Kosko, 1986). CMA has theoretical implications for the understanding of experts and lays cognitive structures and decisional pathways. The results of CMA analysis can also e used for message design and decisional outcome modeling. Many sites explained that symptoms of depression could be side effects of treatment, implying the existence of a positive correlation between patients who receive cancer treatment and experience depression. Practical implications of this include not only meeting with counselors but also meeting with the healthcare team to find out the side effects of a patient's treatment.

Expert Communication about Cancer Clinical Trials: Cognitive Map Analysis
Frantz Garilus, **Sophie Stypelkoski**, Naomi D. Parker, Yulia A. Strekalova
Mass Communication

We are interested in how experts present information about clinical trials including the benefits and risks of participation in cancer clinical trials and the way trials work. Text was coded from NCI-designated cancer center webpages to assess the quality of assertions being made about clinical trials. We then used cognitive map analysis (CMA) to generate further insights. This mixed-methods study employs CMA to identify causal beliefs presented in expert communication. Established in the 1970s (Axelrod, 1976), CMA focuses on cognitive structures articulated in speech or text. It uses systematic textual analysis to identify causal relationships and interconnections among them. Following the initial qualitative stage of analysis, relationships are assessed quantitatively using matrix agenda and network analysis (Kosko, 1986). CMA has theoretical implications for the understanding of expert and lay cognitive structures and decisional pathways. Its results can be used for message design and decisional outcome modeling. An example of a causal linkage found can be noted by the phrase "may be unavoidable." For instance, cancer centers often emphasized that despite efforts to minimize clinical trial risks, some cannot be avoided due to uncertainties associated with new medical treatments. This example and others have implications for trend analysis in expert communication.

Communication about Electronic Nicotine Delivery Systems on Instagram: Using Persuasive Strategies to Talk about #Ecigarettes and #Vaping

Michaela Price, Janeil McCalla, Samantha R. Paige, Janice L. Krieger
STEM Translational Communication Center

The public is introduced to conflicting information about nicotine delivery systems (ENDS; e-cigarettes/vapes). Federal and scientific agencies use image-based messaging to communicate the risks/warnings of ENDS; however, popular image-based social media reaches billions of users worldwide to market ENDS as facilitating a fun and healthy lifestyle. Understanding how image-based social media users communicate mandatory Food and Drug Administration warnings and use persuasive techniques to appeal to users through emotional (humor, fear), social (youth resonance), and credibility features is critical to inform public health campaigns. This study examines which persuasive techniques are used to communicate about ENDS on Instagram. From September to October, we identified 100 Instagram posts. Every three days, keywords "#ecigarettes" and "#vaping" were used to collect 20 posts. Behavior change and social influence theories informed a codebook used by two independent coders. Preliminary data of 20 posts demonstrate that ENDS' risks (20%) are communicated more than benefits (15%). Humor is used to criticize their regulations/bans (10%) and to connect with other ENDS users through pop-culture references (10%). Surprisingly, mandatory FDA labels are only used in the caption of some posts (10%). Findings will demonstrate how image-based social media users employ persuasive techniques to communicate about ENDS.

Zika as an Emotional Rhetorical Device in US Media

Hannah Fechtel, Rebecca Henderson, Marit Ostebo, and Kevin Bardosh.
Anthropology

When the WHO declared Zika a global health emergency in 2016, Zika attracted significant media attention that grew after the CDC announced the link between the virus and the birth defect microcephaly. Despite its failure to spread widely in North America, the Zika crisis was somehow able to maintain US attention consistently for several years. To examine this phenomenon, we conducted a text analysis of articles published by five major news sources between 2015–2018 that involved Zika in their content. The analysis of 153 articles revealed that Zika was the sole focus in only 30% of the articles. In the other 70%, it was used as or in tandem with an emotional rhetorical tool in affect-laden ideas including climate change, women's health, abortion, vaccines, and the Trump presidency. We argue that although Zika possessed enough complexities to make it a worthy news story, its media prevalence can be explained by its use as a rhetorical and affective device in a host of sociopolitical narratives. We suggest that viral assemblage – an analytical concept that merges assemblage theory with Gabriel Tarde's social epidemiology – can be fruitfully applied to understand the relationships formed between Zika and other, seemingly unrelated events.

The Impact of Facial Reduction on Canine Paranasal Sinuses

Ciele Rosenberg, Molly Selba, Valerie DeLeon
Anthropology

Selective breeding in dogs has drastically impacted their cranial morphology. This project compares paranasal sinuses between normocephalic and brachycephalic (short-faced) dogs of similar body size to understand how selective breeding has influenced sinus development. It was hypothesized that there would be a significant difference of volume and surface area between breeds. The sample consists of clinically obtained CT image volumes of normocephalic beagles (N = 10) and brachycephalic English bulldogs (N = 10). The frontal sinuses and maxillary recesses of each dog were segmented out digitally using the post-processing software Amira. Surface area and volume of each sinus were calculated in Amira. Two-tailed t-tests were used to compare values between the two samples. Results of analysis indicated that the surface area and volume of both the frontal and maxillary sinuses are statistically significantly different between brachycephalic and normocephalic dogs. As expected, the maxillary sinuses were smaller in the brachycephalic sample, including volume ($p = 0.003$) and surface area ($p=0.004$). Surprisingly, the frontal sinuses were larger in the brachycephalic sample, including both volume ($p = 0.007$) and surface area ($p = 0.007$). These initial findings illustrate that breeding for aesthetics can have developmental consequence, which merits further research and consideration.

The Uncertainties that Underlie Epidemiological Models – A Closer Look at Reference Usage

Yui Fujii, Marit Ostebo
Anthropology & Center for African Studies

In most cases, epidemiological models are often constructed through data obtained on the field, however, during an outbreak of a newly emerging disease, many are forced to draw on the few papers that exist in the literature to construct their models due to the limited field data. In this study, fifteen epidemiological papers on Ebola, Zika, and Malaria are analyzed to identify the variation of references used to construct their models and to compare how overusing small numbers of references may generate uncertainties. Although all models contain some degree of uncertainty, emphasized in the mantra, "all models are wrong, but some are useful" (Christley, 2013), a greater degree of uncertainty is incorporated by such limited data. The limited data prevents modelers from capturing an accurate portrayal of reality and prevents modelers from validating their models with each other due to the similar inputs that make up their models. This becomes problematic when politicians unaware of the uncertainties embedded within models adopt them to justify policy interventions. Due to the inherent uncertainty of models, modelers must better communicate this underlying issue to policymakers and secondly, greater research needs to be made on how to reduce uncertainties, especially during an outbreak.

Constraining the Star Formation Rate and AGN Fraction in IR-Luminous Merging Galaxies using SED Fitting

Antonio Frigo, Howard Smith, Matthew Ashby, and **John Della Costa III**
Astronomy

Ultra Luminous Infrared Galaxies (ULIRGs) are thought to arise from galaxy mergers in the local universe. The extreme infrared (IR) luminosities originate from both star formation (SF) and merger-triggered accretion onto supermassive black holes, when large amounts of dust absorb and re-emit ultraviolet and optical photons from these phenomena. However, it is difficult to determine which phenomenon contributes most to the IR luminosity in ULIRGs. In this study, we seek to disentangle the light emitted from SF and active galactic nuclei (AGNs) in order to estimate the contributions from each, to better understand the star formation rates (SFRs) in merging ULIRGs, and also to understand the effect of merger stage on them. We use the Code Investigating GALaxy Emission (CIGALE) to fit the Spectral Energy Distributions (SEDs) of the galaxies used in this study. We find that merger stage does not significantly impact the physical characteristics derived from the best fit SED models of the galaxy fluxes. This work will aid future studies in quantifying the various physical processes occurring within merging ULIRGs and help separate the different contributions from their high SFRs and/or AGNs. The SAO REU program is funded in part by the National Science Foundation.

Thermal environments influence the diversity of inhibitory bacteria in three closely related Plethodontid salamanders

Nathalie Alomar, Vincent Farallo, Martha Muñoz, Ana Longo
Biology

Chytridiomycosis, a fungal disease caused by the chytrid pathogen Batrachochytrium dendrobatidis (Bd), has caused the decline of 501 amphibian species. Bd targets the host's skin, making the skin microbiome the first line of defense against this pathogen. In this study, we focused on comparing skin bacteria of three closely-related Plethodontid salamanders (Plethodontid cinereus, Plethodontid sherando, and Plethodontid hubrichti) that differed in their microhabitat preferences, potentially affecting bacterial recruitment. To test this hypothesis, we isolated bacteria from all three congeners (N= 9 per species) by plating the skin swabs of the salamanders. We identified each pure culture of bacteria by extracting DNA, PCR amplifying and sequencing the 16S ribosomal. The results showed P. cinereus had 20 bacterial isolates belonging to six bacterial genera, P. hubrichti had 19 isolates belonging to 12 different genera, and P. sherando had 27 isolates belonging to 14 genera. The two microendemic species harbored a more diverse bacteria assembly within samples. Our findings indicate that these salamanders encounter distinct bacterial species pools, which likely contribute to differences in community structure across microhabitats. By considering the microhabitat of species, we can broaden our perspective about how microbiome diversity of amphibians leads to a more equipped fight against Bd.

Osteoderm Development in Spiny Mouse

Arod Poalnco, Malcolm Maden
Biology

Armor-like Plating on the Tail of the Spiny Mouse Osteoderms, or dermal bones, are plate-like armor that are most prevalent in reptiles but have been discovered in a mammal with extraordinary regenerative capabilities. The Spiny Mouse, Acomys cahirinus, can fully regenerate muscle and skin tissue from almost any injury. The osteoderms that were discovered by CT scan in the Spiny Mouse are only present in two other species of mammals. Recently, we have documented the development of the armor plating of the Spiny Mouse by using immunohistochemistry with the Osterix antibody to dye the cells. Osterix being a transcription factor in bone development. Osteoderm development is like cranial bone development because they both ossify without any cartilage as documented by our immunohistochemistry. H&E stains have revealed that osteoderms in the Spiny Mouse are not fully developed at birth, especially in the distal end of the tail. Development continues several weeks after birth as shown by our H&E time series. Currently we are studying osteoderms by RNA sequencing and hope to discover what genes are expressed to create osteoderms in mammals to compare with reptiles as a model for convergent evolution, along with an interest in studying if osteoderms regenerate.

Investigating the Evolution of Terpene Biosynthetic Pathways in Cultivated Lavender (Lavandula spp.)

Mallory St. Clair, Grant Godden, Pamela Soltis, Douglas Soltis, and Mint Evolutionary Genomics Consortium
Biology

The mint family (Lamiaceae) is a clade of 7,000+ species that produce an array of natural products through specialized metabolism, including mono- and sesquiterpenes. Knowledge of terpene pathways in mints is currently limited, as is our understanding of their evolution. To address these knowledge gaps, we are investigating the genomic basis for terpene biosynthesis in cultivated lavenders (Lavandula spp.), which display considerable variation in terpene types and abundances.

As desirable traits are targeted and proliferate through lavender breeding populations, strong positive selection on genes underlying targeted traits reduces genetic variation in neighboring genomic regions due to linkage, resulting in "selective sweeps" of target and non-target genes. As part of this study, we will explore selective sweeps and aid discovery of genes involved in terpene biosynthesis in a lavender diversity panel exhibiting novel and shared chemistry. We will map resequencing data from accessions of common cultivars and wild populations to a new genome assembly for Lavandula and identify sweep signatures using the open-source software, Raised Accuracy in Sweep Detection (RAiSD). These sweep data will be characterized and correlated with cultivar-specific metabolite profiles, revealing candidate genes and biosynthetic gene clusters associated with specific metabolites and facilitating inferences of their chemical evolution.

Characterization of Stomatal Movement in Enriched Stomata Tape Peels

Nathalia Tello, Shweta Chhajed, Sixue Chen
Biology

Stomata are formed by a pair of guard cells, which are responsible for the movement of the pore. Stomatal movement can create openings through which bacteria can enter. Studying the interaction between stomata and pathogens allows us to understand plant innate immunity (PTI). Stomata tape peels are a new technique for studying single cells. How stomata isolated by tape peels respond to bacteria has not been reported. The main aim of this study was to characterize the stomatal movement phenotype using stomata tape peels following exposure to Pseudomonas syringae pv. tomato DC3000 (PstDC3000). When infected with PstDC3000, the stomata respond by closing within 1h and therefore restricting the infection, reopening after 3h of infection. PstDC3000D28E, a mutant, was also used to observe the reaction. PstDC3000D28E shows no reopening 3h after infection. Time course experiments were performed by infecting isolated stomata from A. thaliana with PstDC3000 and PstDC3000D28E. With PstDC3000, stomata showed normal closure at 1h and reopening at 3h. The mutant showed normal closure after 1h, but no opening after 3h. The isolated stomata reacted the same way leaves do. Overall this study provided insights into the specific involvement of stomata in PTI when there is an external pathogen attack.

Determination of Concentration of Alkyl Lithium Reagents Using Neat Liquids as External References

Jessica Heller, Aditya Kavuturu, Ion Ghiviriga, Adam Veige
Chemistry

The prominence of alkyl lithium reagents in organic synthesis creates need for an easy and reliable method to determine their concentrations. While several reliable methods of traditional colorimetric titration are known, inconvenience deters many laboratories from performing the titrations frequently. Alternatively, NMR can be used to conveniently determine the concentration.

In 2004, Hoye published a method using No-D NMR spectroscopy to accomplish this. The method uses an internal integration standard added to a precisely known volume of alkyl lithium reagent. However, this method can be simplified even further.

Using a neat liquid as an external reference eliminates the need to precisely measure the volumes of reagent and internal standard. The concentration can be determined by simply obtaining separate spectra of the reagent and the neat liquid, without dependence on their volumes. This method was tested by comparing colorimetric titration values to the NMR-determined values for several alkyl lithium reagents.

Design and Synthesize of Au(III) Precursors for Focused Electron Beam Induced Deposition

Thu Kim, Will G. Carden, Lisa McElwee-White
Chemistry

Focused Electron Beam Induced Deposition (FEBID) is a lithographic method that allows one to fabricate 3D metal structures on the nanoscale. In this experiment, organometallic precursors are transported in the gas phase to the deposition chamber where high-energy electron irradiation induces local bond scission of the adsorbed precursor molecules. This results in the deposition of metal-containing structures and the desorption of ligand derived byproducts. Organogold precursors are in high demand as FEBID-fabricated gold deposits provide unique platforms for plasmonic applications. Our previous work centered around designing Au(I) precursors bearing combinations of anionic ligands (Cl, Br, I, CF3) and electron donor ligands (alkylisocyanide, trialkylphosphines, trialkylphosphites, trialkylphosphoramidates). Results from these studies suggest that suppressing intermolecular Au-Au bonding by increasing the size of the anionic ligand improves precursor volatility ultimately leading to the design of CF3AuCNR complexes which are competent for Au deposition. This work focuses on the design and synthesis of four coordinate Au(III) precursors containing two monodentate anionic ligands (halide, perfluoroalkyl) and one bidentate β-ketoiminate ligand. The synthesis of these precursors as well as the effects of the β-ketoiminate ligand on the physical properties of the precursor will be discussed.

Selective Cleavage of Lignin β-O-4 Ether Linkage By Pd/CeO2 Catalyst with Unique Metal-Support Interaction

John Boelke, Zhicheng Luo, Pranjali Naik, Kevin Stewart, Igor Slowing, and Long Qi
Chemical and Biological Sciences at Ames Laboratory

The catalytic activity of heterogeneous catalysts based on noble metals is investigated for the conversion of lignin to precursors of various commodity chemicals. Here we use a model compound containing a β-O-4 ether linkage to understand its cleavage mechanism and kinetics as analogous to that in lignin. It has been found that Pd is the most capable noble metal catalyst tested for β-O-4 cleavage compared to Pt and Ru. The support CeO2 gives the highest selectivity towards acetophenone (rather than hydrogenated products) when compared to other supports. The unique support effects of CeO2 when paired with Pd make it the most effective support. To optimize process temperatures, conversion of the model compound, 2-phenoxy-1-phenylethan-1-ol (PPE) was investigated at 50, 70, 90, and 110 °C under 5 bar H2. When varying the hydrogen pressure between 5 and 50 bar at a constant 80°C, the highest conversion (59%) after 4 hours is achieved at only 10 bar. Our results show interesting insights into the various interactions hydrogen has with aromatic substrates on the surface of metal nanoparticles and lead to the design and optimization of a catalytic reaction that can selectively produce commodity chemical precursors from renewable feedstock, such as polystyrene and Nylon-6.

Developing a Uniform Coating of Carbon Nanomaterials on Large Surfaces by Electrospray Coating

John Veracka, Riley Flanagan, Sahil Ghate, Christopher Rivera, Mounisha Ganesan, Shannon O'Connor
Physical Sciences/Chemistry at Embry–Riddle Aeronautical University

The design, build, and testing of an electrospray platform that can deposit uniform coatings of carbon nanotube solutions (CNTs) across large surfaces is described. Electrospray, also known as Electrohydrodynamic spray or e-spray, is a liquid atomization technique that can generate fine droplets to produce coatings with a high degree of uniformity. Electrospray is used throughout industry and in scientific research; some applications of this process are found in nanomaterials, tissue engineering, pharmaceuticals, medicinal and biomedical applications. The Electrospray platform will be used to apply CNT films, with varying quantities of graphene, that will carry a charge across non-conductive surfaces to act as a de-icing element for aircraft and spacecraft structures.

Opinions on Coral Reef Conservation at the University of Florida

Stephanie Insalaco, Dr. Andrew Noss
Geography

The topic of climate change has become an ever-growing conversation in everyday life. Opinions on the subject vary depending on a person's beliefs as well as their location/proximity to the effects of climate change. One major ecosystem that is being affected by climate change is coral reefs, and this often goes unnoticed because the focus on climate change is mainly on rising temperatures. The University of Florida is a part of northern Florida that does not have a close proximity to coral reefs. Understandably, the population at UF may not be concerned with coral reef conservation because it does not directly affect them. There are efforts at UF that promote environmental conservation and discuss climate change, but it is unknown whether coral reef conservation is included in this discussion. This thesis evaluates the opinions towards climate change and coral reef conservation in Gainesville, Florida through qualitative and quantitative survey data concerning responses to questions about climate change and coral reefs. The data can be used to see what programs or actions concerning coral reef conservation may be helpful if implemented at UF.

Spatiotemporal Effects on Aedes albopictus Wing Length

Emily Stone, Gabriela Hamerlinck, Stephanie J. Mundis, Ari Whiteman, Sadie J. Ryan
Geography

Aedes albopictus mosquitoes are characterized as anthropophilic, aggressive biters and container breeders. These adaptations result in greater population density in areas of lower socioeconomic status (SES), where discarded containers and access to humans are common. This species is a known vector for yellow fever, dengue fever, and Chikungunya. Adult mosquito size is correlated with fitness and their effectiveness as a vector. In Ae. albopictus, wing length has been found to be an indicator of body size and fecundity. We used a collection of Ae. albopictus from Mecklenburg County, NC to identify spatiotemporal patterns of adult mosquito size across SES. Our samples were collected at 90 unique locations in Mecklenburg County from June to August 2017. Wing lengths of 236 adult females were measured and compared across a variety of SES factors and collection month. We found no significant difference in adult female mosquito wing length between SES factors. However, we did find a significant temporal difference in wing length across collection month. The largest females were collected in June, suggesting temperature is important to consider in vector control efforts. These temporal dynamics in mosquito size may be linked to similar trends in vector fecundity and disease transmission potential.

Disease-driven dynamics of evolutionary rescue from a game theoretic perspective
Brandon Grandison, Hannah yin, Ana Kilgore, Jing Jiao, Nina Fefferman
Mathematics

Evolutionary game theory has been used to analyze the stability of competing strategies individuals may employ to withstand selective pressures within a population over generations. Evolutionary rescue, a recently identified phenomenon in which rapid evolution preserves a population that would otherwise go extinct, has not yet been explored using evolutionary game theory. While the initial overall population decline in evolutionary rescue often arises from an environmental change acting as a selective pressure, here, we investigate the intriguing possibility of rescue arising from the special case in which the novel selective pressure is a devastating epidemic. In this scenario, selection appears in the form of differential susceptibility to disease. We therefore couple a game theoretic perspective with an SIR model to understand how such a system might behave. We present an entirely deterministic model that simulates population dynamics of a hypothetical population with a wild type and mutant phenotype. Payoffs from competing strategies come from birth rates that reflect immune-reproductive tradeoffs. We hypothesized that evolutionary rescue can occur when mutants trade relative fitness in disease-free environments for epidemic resistance. Our results confirm this and show that the timescale for evolutionary rescue can vary drastically, requiring further analytical insight to pin down.

Dynamics of Tonic Spiking and Bursting States in Pacemaker Neurons in the Pre-Bötzinger Complex

Muhammad Abdulla, Ryan Phillips, Jonathan Rubin
Mathematics at University of Pittsburgh

This research investigates the mechanisms underlying neuronal bursting. Neurons have been modeled as relatively simple dynamical systems for decades. However, neuronal "bursting," periodic behavior characterized by periods of high frequency spiking alternating with periods of quiescence, is quite complex, and can't be modeled as simply as other behaviors. Multiple parameters, operating on different time scales, i.e. one parameter having significantly faster dynamics than the other, are necessary to model this behavior. (Ermentrout, 2010) In the past, different biological factors, including positive feedback currents (Butera, 1999), dynamic ion concentrations (Barreto, 2010), and different experimental conditions (Bacak, 2016), have been incorporated into mathematical models to capture various aspects of neuronal bursting. This paper proposes a mathematical model that includes both dynamic ion concentrations and positive feedback via persistent sodium currents, to model neuronal bursting under physiological conditions. Bifurcation analysis of this autonomous dynamical system offers insights into the mathematical mechanisms underlying biologically observed solutions, in which neuronal activity gradually evolves from sparse tonic spiking to full bursting, as well as other activity patterns emerging as neurons transition into the bursting state.

Crime, Punishment, and Mental Disability: An Investigation of Madison v. Alabama
Aimee Clesi, Dr. Jaime Ahlberg, and Dr. Steven Noll.
Philosophy

On February 27, 2019, the Supreme Court of the United States issued a landmark decision in the case of Madison v. Alabama, redefining the scope of the Eight Amendment prohibition of cruel and unusual punishment. In April of 1985, Vernon Madison shot and killed police officer Julius Schulte and was later found guilty and sentenced to death. As a result, Madison has been on death row in Alabama for over 30 years. Madison's physical and mental health have severely declined, and he has experienced several debilitating strokes, which have left him unable to remember committing the crime for which he is to be executed. Madison's case raises questions for philosophy and history; namely, (1) What philosophical theories best explain whether to impose the death penalty, especially in a case like Madison's? (2) What is the relationship between personal identity and the self? Is Madison the same person now that he was when he committed murder in 1985? and (3) What history surrounds mental health and disability in the United States court system, considering capital punishment, according to legal precedent? This presentation is focused on descriptive, historical, and philosophical research and aims to discuss possible answers to these questions.

Detection of Phase Transitions in Phase Separated (La1-yPry)1-xCaxMnO3 Thin Films

Jonathan DeStefano, Amlan Biswas
Physics

Phase separated manganites have competing phases that each have unique electronic, magnetic, and structural properties. The similar free energies these phases possess allow for the manipulation of phase transitions with the application of external stimuli. Here we report the role of an external magnetic field and a change in chemical doping ratios on the phase transitions in (La1-yPry)1-xCaxMnO3 thin films grown on NdGaO3. These thin films showed that the nucleation and growth of ferromagnetic metallic regions in an anti-ferromagnetic charge ordered insulating background occurs at a higher temperature when an external magnetic field is applied. At a high enough field strength, these ferromagnetic metallic regions hinder the anti-ferromagnetic charge ordered insulating to paramagnetic insulating phase transition that occurs at a relatively high temperature (close to 200 K). The value of the activation energy for the anti-ferromagnetic charge ordered insulating phase calculated by fitting the resistance vs. temperature data to the Arrhenius equation agrees with direct measurements taken using scanning tunneling spectroscopy.

Using Machine Learning to Identify New Particles in the Decay of the Higgs Boson

Ariana Gonzalez, Lucien Lo, Darin Acosta
Physics

The Higgs boson in the Standard Model is a particle that couples to other particles in proportion to their mass, thereby defining that mass for each particle. There could be new fundamental forces that are propagated by other boson particles that also have mass. This research attempts to improve a neural network that enhances the search for these new particles in Higgs boson decays. This analysis uses proton-proton collision data from the CMS detectors of CERN's Large Hadron Collider to search for the Higgs boson decay channel to a Z boson and a new particle (Z-prime boson) in four lepton final states. The leptons considered are electrons and muons. This analysis achieves its goal by training on more lepton kinematic variables via machine learning. Machine learning maximizes the discrimination of the signal process of Higgs to Z+Z-prime bosons from other backgrounds with a similar final state. This involves creating the new variables, making plots for these new variables, and testing the performance of the neural network with the new variables added. The reported results by adding these new variables are the improvement of the neural network's accuracy and performance, which aids the search for this new Z-prime boson.

Changes in the Magnetic Response of a Haldane Gap Material due to Aging

Alisha M. Patel, Orlando Trejo, Benjamin L. Soldo, John M. Cain, Mark W. Meisel
Physics

This project was undertaken to expose the student to experimental physics and to investigate a topic of interest to the senior investigator. A study of the Haldane gap [0] material NINAZ from 1998 was conducted to search for possible aging effects of the material and to investigate whether it could be a potential magnetocaloric refrigerant, a material that changes temperature when in a varying magnetic field. A DC SQUID magnetometer was used to collect data of three aged NINAZ samples that Granroth [1,2] used in 1998. The data clearly indicate the magnetic properties of NINAZ have changed significantly and that long range ordering is now present in the aged samples.

Flip the Pic: Orientation and Emotion in Natural Scene Processing

Rachel Martin, Claren Anderson, Dr. Margaret Bradley
Psychology

Previous research indicates that unpleasant, compared to pleasant, scenes evoke faster reaction times when people make speeded decisions about picture pleasantness, although these decisions are fairly slow. This study investigates whether the same pattern is found when decisions lack emotionality. For each trial, participants were instructed to rapidly decide whether an image included people or not and press one of two buttons. Pictures were pleasant, neutral or unpleasant, and some were presented inverted to delay perceptual processing. A dense sensor electroencephalograph (EEG) net was attached to measure and record neural activity throughout the decision-making process. Results indicated that decisions were much faster when emotionality was not part of the decision. Both affect and image orientation impacted reaction time. As expected, reaction time for inverted images was slower than for upright images. Unpleasant images now elicited the slowest reaction times, regardless of orientation. Neural activity varied with both orientation and affect. Taken together, the data indicate that although sheer perceptual processing of unpleasant images requires more time, people are generally faster to identify these cues as aversive. These data are consistent with theories of natural selective attention which propose that stimuli cueing threat and danger are a priority for living organisms.

Rural Youth's Self-Reported Substance Use and Living Situation

Analiese Morales, Gabriella Escobar, Madeline Arlinghaus, Syed Muhammad Omar, Allison Metz, Sarah Lynne, and Julia Graber
Psychology

Recent research in urban environments shows that a higher percentage of homeless youth report substance use compared to traditionally housed youth (i.e., housing situation with a residing caregiver; Haber & Toro, 2004). Urban foster youth also experience higher vulnerability to substance use compared to traditionally housed youth (Zahn et al., 2016). Substance use has been implicated as a coping mechanism for psychopathologic symptoms such as anxiety, anger, or depression, which have been observed to be more prevalent among homeless and foster youth (MacLean et al., 1999; Saperstein et al., 2014). Thus, we expect there may be differences in substance use among these three populations (homeless, foster, and traditionally housed youth) in our rural early adolescent sample, with homeless and foster youth reporting more substance use than traditionally housed youth. Gender differences are not expected (Laurel et al., 2010). This study aims to compare rates of self-reported substance use by housing situation (homeless n=29, foster n=129, and traditionally housed n=2,210) among middle school youth (n=2,399; age M= 12.64, SD = 1.33; 50.7% female; 42.9% White) from a rural Southeastern county in the United States. This evaluation aims to extend previous research.

Does Oxytocin Prevent Cocaine-seeking in the Rat Due to its Ability to Increase Extracellular Glutamate in the Nucleus Accumbens?

Giselle Rojas, Carly Logan, Lori Knackstedt
Psychology

Treatment with exogenous oxytocin has been shown to attenuate cocaine relapse in the extinction-reinstatement animal model of relapse. We tested the hypothesis that systemic administration of oxytocin would also increase glutamate levels in the NAc of both sexes. Because oxytocin reduces relapse in both sexes, we predict there wont be sex differences in this glutamate increase. We surgically implanted bilateral cannulae aimed at the NAc. On the day of testing, we inserted a microdialysis probe into the NAc of one hemisphere. After collecting baseline samples, we injected rats intraperitoneally (IP) with sterile saline and collected samples. Later administering oxytocin (1 mg/kg, IP) and collected samples for an additional two hours. We quantified glutamate levels via HPLC, comparing glutamate concentration during baseline and after systemic injection of oxytocin. We observed a significant change from baseline and oxytocin-evoked glutamate release in female rats compared to the male rats. We will next conduct the same experiment in cocaine-experienced rats. Our findings suggest that oxytocin may differentially affect brain glutamate, implying that the mechanism by which oxytocin alters behavior levels could depend on gender.

Examining Living Situation and Adult Supervision as they Relate to Rural Adolescents' Sexual Health

David Zollicoffer, Brianna Fleming, Carolina Bou, Madeline Arlinghaus, Omar Syed, Allison S. Metz, Sarah D. Lynne, and Julia A. Graber
Psychology

Homeless adolescents are at higher risk of engaging in sexually risky behaviors than those in traditional living environments (Martino, 2011). Prior research shows sexual victimization, sexual assault, and prostitution occur at high rates amongst homeless youth (Herdee, 2015) and homeless youth also have a higher prevalence of STIs than those in traditional living environments (Halcon, 2004). One potential explanation is that homeless adolescents lack adult supervision compared to traditionally housed adolescents (Toro, 2007), which is correlated with increased sexual behaviors and sexual risks (Cohen et al., 2002). This study aims to compare homeless adolescents with adolescents in traditional housing to see if there are differences in adult supervision and sexual risk factors. Specifically, we hypothesize homeless youth will report less adult supervision than traditionally housed youth, and that homeless youth will report greater intent to have sex and less knowledge about STI/HIV infection and transmission compared with traditionally housed peers. Data were collected from 2,399 adolescents (n=29 homeless) during a pregnancy prevention program conducted at rural middle schools in the Southeastern U.S. (Mage=12.64, SD=1.33; 50.7% female). 42.9% of the sample identified as White, 16.8% as Black, and 42.6% Hispanic.

Gender and Professional Identity of Judges

Charlotte Tuohy and Marian Borg
Sociology and Criminology

This research explores the relationship between gender and professional identity among female county court judges. The data are derived from a larger project examining judicial decision-making, judicial philosophy, and identity issues among 25 county court judges in Florida. Preliminary analysis of in-depth interviews with 3 female judges suggests the importance of examining how gender and professional identity interact. Analysis of the data has led to the emergence of three key themes that will form the basis of further study: 1) How do female judges understand the relationship between their professional and family roles; 2) How do they manage their identity as female judges in the courtroom and through their courtroom demeanor; and 3) How does their gender interact with the relationships they have with male colleagues? These questions will be examined within the context of more general sociological literature examining gender roles and gender identity in other professional workplaces. The goal will be to discuss similarities and differences between the experiences of female judges and women working in other professional environments.

Nrf2 deficiency exacerbates cognitive impairment and reactive microgliosis in lipopolysaccharide-induced neuroinflammation mouse model

Alexandra Mazur, Lei Liu, Marie Kelly, Xiao Yang, Tyler Fernandez, Erika Wierzbicki, Anna Skrobach, Anthony Castro, Dirk Hoening, Wade Munger, Afsara Purba, and Sylvain Doré
Anesthesiology

The transcriptional factor Nrf2 is a central regulator of anti-inflammatory mechanisms that contribute to the development and progression of different neurological disorders. Although the direct and indirect regulatory roles of Nrf2 on neuroinflammation have been well reviewed in recent years, the in vivo evidence of Nrf2 function on lipopolysaccharide (LPS)-induced characteristic alternations of reactive microglia and astrocytes and subsequently cognitive decline remain incomplete. After saline or LPS injection, the male C57BL/6 WT and Nrf2-/- mice aged at 5-6 months were subjected to novel object recognition task. The immunohistochemistry staining was employed for morphological analysis of brain cells. It was shown that the Nrf2-/- mice displayed exacerbated LPS-induced cognition impairment, enhanced hippocampal reactive microgliosis and astrogliosis, and increased expression level of hippocampal water channel transmembrane protein aquaporin 4. In addition, similar effects of Nrf2 on LPS-induced characteristic alternations of brain cells were also observed in the cortex and striatum regions of mice. In summary, this transgenic loss-of-function study provides direct in vivo evidence that highlights the functional importance of Nrf2 in regulating LPS-induced glial responses, cognitive decline, and AQP4 expression. This finding increases the understanding of the complex nature of Nrf2 signaling that has significant importance for potential Nrf2-based therapeutics.

Role of the Prostaglandin E2 (PGE2) receptor subtypes EP1, EP2, and EP3 in repetitive traumatic brain injury

Krunal Shukla, James Catlin, Jenna L. Leclerc, Sarah M. Marini, Sylvain Doré
Anesthesiology

The goal is to explore the signaling pathways of PGE2 to investigate therapeutic effects against secondary injuries following TBI. Young (4.9±1.0 mo) and aged (20.4±1.4 mo) male wildtype (WT) and PGE2 EP1, 2, and 3 receptor knockout mice were selected to either receive sham or repetitive concussive head injury. Immunohistochemistry protocols were performed to evaluate hippocampal microgliosis and astrogliosis, two critical components of neuroinflammation. Passive avoidance test measured memory function associated with the hippocampus. No differences in hippocampal microgliosis were found when aged EP2-/- and EP3-/- mice were compared to aged WT mice. However, the aged EP1-/- mice had significantly less microgliosis in the contralateral hemisphere compared to aged WT mice. Compared to aged EP2-/- and EP3-/- mice, aged EP1-/- mice had significantly less microgliosis in the contralateral hemisphere. Aged EP1-/- mice had significantly less microgliosis compared to EP1-/- young mice in the contralateral and ipsilateral hemispheres respectively. There were significant differences in latency time within EP1-/-, EP2-/-, and EP3-/- on day 1 and day 2 in aged and young mice. These findings demonstrate that the PGE2 EP receptors may be potential therapeutic targets to treat repetitive concussions and other acute brain injuries.

Temporal Interference Stimulation for Magnetic Resonance Imaging

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Biochemistry and Molecular Biology

The ultimate goal of this project is to study the distribution of focused stimulation of electric current flow in the brain using magnetic resonance imaging. Electric stimulation of the brain may be useful in stroke rehabilitation, epilepsy treatment, and improvements of cognitive performance, but current methods are not well suited to specific brain regions. Recently a focused stimulation method was introduced, which uses temporally and spatially interfering electric fields, to focus the location of stimulation in the brain without stimulating other brain regions.

Current density distributions and conductivity in the brain can be reconstructed using a method called magnetic resonance electrical impedance tomography (MREIT), a capability recently demonstrated in humans. We can use MREIT to visualize temporally interfering electric field currents.

We have been working on simulating these temporally interfering electric fields for three experimental setups with spatially distributed electrode pairs, evaluating the current distribution of each and its suitability for further usage. The simulated data has matched the theoretical expectations accurately, and is indicative of the best experimental setup to verify it.

Further research will include experiments on phantoms and in humans, using MREIT to visualize the current.

Cardiac Stem-cell Therapy in the Field: Under Regulated, Under Observed, Poorly Understood

Amanda Lindeman, Carl Pepine, Keith L. March
Cardiology

Introduction: A large body of anecdotal information exists on cellular therapies with limited high-level evidence on their efficacy. Because of regulatory hurdles, a growing number of clinics in the USA offer stem-cell therapy without FDA approval. Florida has been identified as a hotspot for these clinics. To understand the magnitude and scope of this issue, we surveyed clinics in Florida that advertised stem-cell treatment for heart failure.

Methods: Using several search strategies, we identified a total of 76 clinics, 8 of which treat heart failure. Data on cell type, persons performing procedures, dose, administration, cost, and success rates were collected when available.

Results: A total of 20,135 patients were treated, 2,157 of them for "cardiac conditions." Cells were administered intravenously, using adipose or umbilical-derived sources. Doses ranged from 30 to 150 million cells. Success ranged from 65% to 85%, with costs from $6,000 to $20,700.

Conclusions: While stem cells are increasingly attractive to both patients and providers, research and FDA regulations are evolving slowly in this booming direct-to-consumer market. As significant numbers of patients were treated for "cardiac conditions," implementation of uniform data collection would be most useful to both patients and the cardiovascular field at large.

Cardiac Fibroblasts Exposed to Triple-Negative Breast Cancer Cells Secretome Have a Different Response to Doxorubicin

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Anthracyclines remain an essential curative component of adjuvant treatment for triple-negative breast cancer (TNBC), but their cardiotoxic side effects offset the beneficial anti-tumor effects. Previous studies are limited by not employing animal models with cancer. Our prior studies indicate that cancer patients experience myocardial damage before initiating chemotherapy. We wonder if the presence of tumors predisposes the heart to become susceptible to cardiotoxicity. We sought to determine the effects of TNBC mouse secretome on cardiac fibroblasts before, during, and after doxorubicin (Dox, a widely used anthracycline). Cardiac fibroblasts were randomized to TNBC or DMEM (control) media for 24-hours and exposed to increasing concentrations of Dox 24-hours later. After Dox exposure, all media was replaced with DMEM. These steps recapitulate a clinical situation where cardiac cells are initially exposed to the secretome of TNBC, treated with Dox and recovered. At 24-hours post-Dox treatment/removal, cardiac fibroblasts in TNBC media treated with 1-μM Dox exhibited significantly lower cell-index levels compared to those in DMEM ($p=0.01$ and $p=0.01$, respectively). Dox differentially affects cardiac fibroblasts exposed to TNBC secretome. These data suggest other cardiac cells (i.e. cardiomyocytes) may respond differently to Dox treatment in in-vivo tumor models of cardiotoxicity.

Targeting microglia in mouse brains using recombinant AAV vectors

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Center for Translational Research in Neurodegenerative Disease

In the past, recombinant adeno-associated viruses (rAAV) have been applied in gene therapy approaches that address the central nervous system (CNS), and specific cells such as microglia, the target of this experiment. This experiment will examine the application of self-complementary AAV (scAAV), paired with a CD68 promoter to examine the efficacy of 27 different capsids on transduction and expression in microglia cells. The CD68 promoter has been proven to be an effective microglia-specific promoter in the past, and was chosen for its ability to target microglia cells, which are notoriously difficult to permeate. Furthermore, each rAAV genome was self-complementary, and double-stranded. The 27 capsids being tested were chosen from the library available to us, and many were developed in-house with the intention of transducing various cell types within the brain. The 27 AAV preparations were subsequently injected in neonatal wild-type mice upon birth, using intracerebroventricular injections. After a period of 15 days and 30 days, the brains were harvested, then embedded in paraffin, processed using immunohistochemical techniques and examined under an EVOS microscope for expression. The results of this experiment serve as a guide to the 27 capsid types and their extent of expression seen in microglia cells.

Estimation and Inference for High Dimensional, Doubly-structured Regression Models

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Clinical Biostatistics at Fred Hutchinson Cancer Research Center

Popular regularized regression models, such as the LASSO and Ridge regression, are unable to incorporate additional structural information into the fitting procedure. This is a disadvantage when variables in the model are highly correlated, as is often the case when analyzing high-throughput biological data. Kernel Penalized Regression (KPR) is an extension of Ridge regression that fits models with respect to variable and subject structure. We have developed an R software package for fitting KPR models and performing inference on the estimated coefficients. To select model tuning parameters, we have implemented both cross validation and Restricted Maximum Likelihood estimation via a mixed model formulation. The package also includes helper functions for data processing and visualization with a supervised biplot. An analysis of microbiome bacterial abundance data with the KPR model showed that the inclusion of structural data can improve model interpretability and statistical power, leading us to conclude that our package can provide great utility to researchers analyzing highly structured data.

Understanding the Anticancer Mechanism of Disulfiram, Copper, and Etoposide in Merkel Cell Carcinoma

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Merkel cell carcinoma (MCC) is an aggressive, rare neuroendocrine skin cancer with two subtypes based on Merkel cell polyomavirus status. Effective treatments for this cancer are limited, therefore, our group conducted a high-throughput drug screen to identify drugs which would selectively reduce MCC cell viability. Our drug screening results showed that disulfiram, an aldehyde dehydrogenase inhibitor used in the treatment of alcoholism, was highly effective in selectively reducing MCC cell viability. The addition of copper at physiological levels augmented the potency of disulfiram in all MCC cell lines. Furthermore, DSF plus copper synergized with etoposide, a topoisomerase II inhibitor which is currently a chemotherapeutic treatment for MCC, to further reduce MCC cell viability. These observations drove us to conduct an in vitro study of the anticancer mechanisms of disulfiram, copper and etoposide for the treatment of Merkel cell carcinoma. Mechanistically, combining DSF, copper and etoposide did not induce apoptosis in MCC cell lines but did increase the expression of γH2A.X, the cell size and the presence of autophagosomes, which is an indicator of immunogenic cell death. Taken together, our data suggest that disulfiram combined with copper could be repurposed for the safe and effective treatment of MCC.

Novel Drug Treatment for IBD

Christopher Broxson, Ellen Zimmermann, **Chase Trunnell**
Gastroenterology

Background: Inflammatory bowel disease (IBD) encompasses two chronic lifelong inflammatory diseases of the gastrointestinal tract, Crohn's disease (CD) and ulcerative colitis (UC), that have no cure. The family of enzymes known as phospholipase A2 (PLA2) are significantly elevated in the inflamed tissues of IBD patients.
Hypothesis: The increased expression of PLA2 at sites of inflammation may be useful to liberate an otherwise inactive conjugated drug at the exact sites needing treatment.
Methods: We used Caco-2 intestinal epithelial cells in a standard cell culture environment, and stimulated them with the cytokine IL-1β to mimic the inflammatory environment of patients with IBD. We first did a viability assay to verify functional doses of IL-1β that were not cytotoxic. We then exposed cells to 10 ng/ml of IL-1β for 24 hours and harvested cellular mRNA to analyze for increased PLA2 gene expression using quantitative polymerase chain reaction (qPCR).
Results: PLA2G2a mRNA was detected in Caco-2 cells, however IL-1β treatment did not significantly increase gene expression of PLA2G2a.
Future directions: While PLA2G2a expression was not increased by exposure to IL-1β, post transcriptional mechanisms may still play a role, so we have isolated intracellular protein to confirm our results by looking a protein expression.

Behavioral Corrections of Mucopolysaccharidosis type III B (MPSIIIB) through AAV8 Vector Gene Therapy

Aishwarya Kunta, Kimberly Hawkins, Coy Heldermon
Hematology/Oncology

Mucopolysaccharidosis type III B (MPSIIIB) is a lysosomal storage disease. It develops in the absence of the alpha-N-acetylglucosaminidase (NAGLU) enzyme, and causes a buildup of heparan sulfate, in all cells. Patients with this genetic disease experience severe neurodegeneration which is reflected in behavioral issues such as erratic sleep cycles, loss of mobility, and hearing impairment. There is no cure for this disease. Current clinical trials focus on increasing NAGLU in the brain in order to ameliorate these behavioral defects. Our lab aids in this research by studying CNS injections of viral mediated gene therapy. We hypothesized that a triple capsid mutated AAV8 (TCM8) treatment will enhance transduction efficiency into the CNS and will be reflected in the correction of the behavioral problems associated with MPSIIIB. We are also testing the effectiveness of two different methods of delivery, the intercranial 6-site injection (IC6) and the cisternal magna injection (ICM). Although the project is ongoing, the data we have collected from running wheel, rotarod, and auditory brainstem response (ABR) tests show a correction of behavioral responses of TCM8 treated mice. Specifically, TCM8 treated mice tend to have a higher hearing threshold and a more regular circadian rhythm than those of mutant mice.

Analysis of Co-Stimulation in Anti-PSCA CAR-T Cells for Pancreatic Cancer

Zara Hedaya, Emiliano Roselli PhD, Daniel Abate-Daga PhD
Immunology at Moffitt Cancer Center

T Cell immunotherapy involving the enhancement of a patient's immune cells to fight cancer has been established as a clinically proven strategy in treating various malignancies. Presently, there are limited options in the types of solid tumors in which T cell Immunotherapy treatment can be clinically applied, so researchers have focused on developing adoptive methods that can effectively target a wide range of cancers while preventing cross reactivity and off-tumor toxicity. The Chimeric Antigen Receptor, or CAR, was developed as a T-cell-based immunotherapy method in which T Lymphocytes are genetically engineered to express a synthetic receptor that is able to directly recognize tumor antigens. Without surface expression of the CAR, a conventional T cell Receptor would require an MHC (Major Histocompatibility Complex) molecule, something often down-regulated by tumor cells, in order to bind a tumor antigen and recognize the cell as non-self. Various CAR configurations were tested in-vivo, with adjustments made to the intracellular signaling domain of each construct. The efficiency of each construct was then tested against a human pancreatic cancer (HPAC) cell line, and it was found that the CAR construct containing the CD-28 co-stimulatory protein yielded the greatest anti-tumor effect.

Human Norovirus Replication Optimization in 293T Cells with Ruxolitinib

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Molecular Genetics and Microbiology

In this experiment, we were trying to optimize human norovirus replication in human 293T cells. The cells were infected with human norovirus and were tested if adding Ruxolitinib drug to the cultured cells to determine a noticeable difference in virus replication. Ruxolitinib is a kinase inhibitor that has side effects that allow for opportunist infections. The experiment is testing if adding Ruxolitinib would cause more infection in the 293T cells. The cells, once infected with human norovirus, remained under incubation for 3 days to allow for maximum replication possible. Once these cells completed incubation time, the RNA was extracted from each sample. The RNA were then ran through a qRTPCR to obtain a quantitative value for the virus replication. After the protocol was finished, there was no clear difference between the virus replication of the samples with and without the Ruxolitinib.

Effect of Ammonia on Vasodilation Regarding Hepatorenal Syndrome

Yuan Li, Rajesh Mohandas
Nephrology

Cirrhosis, a progressive fibrotic liver disease, is often associated with elevated ammonia levels, hypotension due to systematic vasodilation, and risk of kidney failure (hepatorenal syndrome). However, the role of ammonia in the systemic vasodilation is unknown. We hypothesized that ammonia directly acts on vascular smooth muscle cells to cause vasodilation. Methods: First-order, mesenteric arteries were isolated from 16-week-old male C57BL/6 mice, and arterial function was studied in pressure arteriography. Arteries were equilibrated at 60 mmHg in physiological buffer. The effect of ammonia was assessed by adding ammonium bicarbonate and ammonium chloride in increasing doses to vessels pre-constricted to 50% of initial luminal diameter with phenylephrine. Endothelium independent effect was assessed by using an inhibitor of inducible nitric oxide synthase along with ammonia. Results: Our preliminary data shows ammonia is a vasodilator at doses ranging from 10^-5M to 10^-1M. The maximal dilation was 44.32%. This vasodilatory effect was unchanged by iNOS inhibition suggesting a direct effect on vascular smooth muscle cells. Conclusion: Ammonia acts directly on vascular smooth muscle cells lining the blood vessels to cause vasodilation. Hyperammonemia might have a role in hypotension in patients with cirrhosis and predispose to hepatorenal syndrome.

Studying Biological Role of Tie2 in Vascular Endothelial Cells

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Nephrology at Northwestern University

The Tie2 receptor is expressed on vascular endothelium and regulates angiogenesis and blood vessel quiescence. Mutations in the Tie2/TEK gene have been linked to venous malformations and primary congenital glaucoma. To overcome embryonic lethality observed in conventional Tie2-knockout mice, we generated a conditional knockout mouse model for Tie 2 (Tie2-flox/flox). To investigate the postnatal role of Tie2 in endothelial cells, we used Chd5-Cre/ERT2 (Vascular Endothelial [VE]-Cadherin-Cre/ERT2) mice expressing the Cre-ERT2 fusion gene under the endogenous VE-cadherin (Cdh5) gene promoter. When Cdh5-Cre/ERT2 mice are bred with mice containing a loxP-flanked sequence of interest, tamoxifen-inducible Cre-mediated recombination will result in deletion of the flanked sequences in Cdh5-expressing vascular endothelial cells. Here, Tie2 iEC-KO mice were generated by breeding Cdh5-Cre/ERT2 mice with Tie2-flox/flox mice. Postnatal tamoxifen injections were administered to three-week-old pups on three consecutive days. A week later, multiple tissues were harvested and Tie2 expression analyzed by Western Blot and immunohistochemistry. Antibody staining demonstrated successful deletion of Tie2 from the endothelium in tamoxifen-treated Tie2-flox/flox, Cdh5-Cre/ERT2 pups. This new mouse model will be valuable to study the biological role of Tie2 in multiple organs and disease states at any embryonic or adult stage.

A large-scale RNAi screen in Drosophila unravels genetic modifiers of human TDP-43 toxicity

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Neurology

Lou Gehrig's disease currently affects 30,000 people in the US. TAR DNA-binding protein 43 (TDP-43) is associated with Lou Gehrig's disease and front temporal dementia. There is a need to find effective treatments for these devastating disorders. A key challenge is identifying critical proteins and pathways that mediate TDP-43 insults. Drosophila models have reliable and easy-to-score phenotype in the eye. Using genetic modifiers expressing human TDP-43, crossing it with a next-generation library of 6,484 RNAi strains to assess the effect of silencing individual targets. Genes that suppressed the eye phenotype were catalogued as pathogenic factors, while those that enhanced were catalogued as potential neuroprotectors. We identified almost 300 modifiers of mutant TDP-43 toxicity in a primary screen. To date, there have been confirmed 100 robust suppressors, 80 enhancers and 20 lethals. In summary, this loss-of function genetic screen has led to the identification of several genes and molecular pathways not previously known to be associated with TDP-43 pathologies. The results will provide novel therapeutic targets to approach the devastating TDP-43 proteinopathies and will reveal which pathways could be targeted for better efficacy.

The role of BTBD9 in the cerebral cortex and the pathogenesis of restless legs syndrome

Shangru Lyu, **Keer Zhang**, and Yuqing Li
Neurology

Restless legs syndrome (RLS) is a nocturnal neurological disorder affecting up to 10% of the population and is characterized by an urge to move and uncomfortable sensations in the legs. Previous research identified BTBD9 as a genetic risk factor of RLS and suggests a thinner brain tissue in the primary somatosensory cortex (S1) might associate with RLS symptoms. However, the role of cerebral cortex in the pathogenesis of RLS remains unclear. To explore this, we compared the morphological changes in Btbd9 knocked out (KO) and cerebral cortex-specific Btbd9 KO mice (Btbd9 cKO). We prepared the brain slices using histological method and compared the thickness of corpus callosum, primary somatosensory (S1) and motor cortex (M1) between the Btbd9 KO or cKO mice and their wild type or control littermates. The cKO mice allowed us to have an accurate and targeted effect with loss of Btbd9 in only the cerebral cortex. Our result showed both Btbd9 KO and Btbd9 cKO mice had 1). thinner S1HL that may correlate with sensory deficits and 2). thinner M1 that may correlate with motor deficits. We concluded that cerebral cortical BTBD9 deficiency alone is sufficient to induce both behavioral and morphological phenotypes in RLS patients.

Age-Associated Decrease in Hippocampus CA3-CA1 Ripple Coordination

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Neuroscience

Our aging population continues to grow, and because of the correlation between age and memory impairment, we are expected to see epidemic levels of cognitive decline. Previous studies indicate that the pathway between hippocampal subregions CA3 and CA1, known as the Schaffer Collateral, exhibits a decreased synaptic efficacy in aged, memory-impaired rats. This finding, along with evidence for CA3 hyperexcitability found in age-associated, memory-impaired rats, non-human primates, and humans, suggests that the hippocampus is involved in this cognitive deterioration. It, therefore, becomes increasingly important to understand functional changes in the brain associated with this cognitive decline. To better understand how CA3 activity impacts that the CA1 during aging, we recorded in vivo extracellular local field potentials from the right CA1 and CA3 hippocampal subregions of young and aged rats. Recordings took place while rats performed a task focused on object discrimination; a task on which aged animals have previously exhibited diminished performance. We hypothesize that the CA3 and will show a reduction in its ability to influence CA1 activity as a result of the degradation of the Schaffer collateral pathway. Through this research, we aim to illuminate the impact of advanced age on hippocampal dysfunction and cognitive decline.

Phrenic Neuropathy in Trembler J Mice

Hannah Bazick, **Alexa Mealy**, **Malavika Nair**, Jonathan Larochelle, Ethan S. Benevides, Michael D. Sunshine, Daniel Grey, Darin J. Falk, David D. Fuller, Lucia Notterpek
Neuroscience

Charcot-Marie-Tooth disease type 1A (CMT1A) and Dejerine-Sottas disease (DSS) are demyelinating diseases of the peripheral nervouSs system that cause respiratory complications. Trembler J (TrJ) mice carry a point mutation in peripheral myelin protein 22 (PMP22) and serve as a model of DSS. We hypothesized that phrenic nerve degeneration leads to destabilization of the NMJ and contributes to respiratory dysfunction in TrJ mice. Quantifying multiple morphological parameters from the phrenic nerve of wild type (Wt) and TrJ mice revealed highly significant demyelination and axonal atrophy in affected samples. Analyses of muscle atrophy gene transcript levels detected a significant down-regulation in affected mice. Protein levels for the same muscle atrophy markers remained stable, suggesting impaired protein turnover. Unexpectedly, we identified significant enlargement of myofiber cross-sectional area in the diaphragm from TrJ vs. Wt mice. We examined breathing patterns using whole body plethysmography, and the results suggest changes in the control of breathing in TrJ mice. Our findings suggest that severe phrenic nerve neuropathy contributes to NMJ degradation in neuropathic animals, causing detectable changes in myofibers of the diaphragm. Further elucidating the mechanisms contributing to respiratory dysfunction in neuropathic models will identify appropriate tissue targets for treatments to improve patient quality of life.

Evaluating gene expression of rAAV serotypes in vivo using novel AAV production method

Catalina Mejia, Marshall Goodwin, Daniel Ryu, Xuefei Liu, Kefren Arjona, Gia Paterno, Sanjana Bhargava, Pedro E. Cruz, Yona Levites, Todd E. Golde
Neuroscience

Adeno-associated virus (AAV) mediated gene expression provides the potential for a powerful gene delivery system to treat neurodegenerative disease. Transduction of recombinant AAV (rAAV) has shown varying efficiencies according to serotype due to tissue targeting. This study involved packaging rAAV2-EGFP vectors in various wild-type and mutant capsids via PEI-based 293T transfections. We utilized a novel method of rAAV production, from the media of transfected 293T HEK cells. Virus was delivered directly into the ventricles of neonatal mice brains. Using unpurified virus in this way circumvents the time and cost associated with producing pure rAAV, with the expectation of achieving comparable gene expression to pure virus. Secreted media was titrated showing sufficiently high concentrations. Transduction efficiency was then evaluated in brain slices, (as reflected in serotype expression) helping to further legitimize this production method. Transduction occurred at high levels, with rAAV2/8 having the highest transduction efficiency overall. AAV82/8-3Y packaged with mIL6 and mIL10 transduced CNS organs and many peripheral organs. Antibodies IBA1 and GFAP detected an immune response in these tissue samples, additionally illustrating serotypes' ability to enact a bioactive effect in the CNS. These findings collectively indicate the utility of unpurified virus during various stages in rAAV research.

Encoding and enhancement of the motivation to consume alcohol by the central nucleus of the amygdala

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Neuroscience at Johns Hopkins University

Alcohol use disorder is characterized by high rates of relapse even after long periods of abstinence and poses significant threats to personal and societal well-being. Previous studies have shown the central nucleus of the amygdala (CeA) to be implicated in the transition from recreational alcohol intake to compulsive drinking and to play an important role in enhancing the attractiveness of a drug. However, it is not yet clear how the neurons in this region contribute to alcohol intake in behaving animals. We used in vivo electrophysiology and optogenetic manipulation in Long-Evans rats in a free drinking paradigm to investigate CeA neural responses to alcohol intake in order to better understand the ways by which neurons in this region contribute to compulsive alcohol drinking. In the electrophysiology portion of this study we found that a subset of CeA neurons were coherent with lick responses, suggesting that the CeA contains neurons that drive alcohol consumption. Meanwhile, our optogenetic stimulation of the CeA during consumption of alcohol in a closed loop design shows that CeA stimulation paired and time-locked to consumption increased alcohol intake. Overall, these findings indicate that the CeA is engaged to promote alcohol consumption prior to development of physical dependence.

The Utility of a Smartphone-Based Retinal Imaging Device as a Screening Tool in an Outpatient Clinical Setting

Victor Sanchez, Ajay Mittal, Luz Mata, Nikhil Patel, Karthek Ramchander, Rafael Robles, Keer Zhang
Ophthalmology

Smartphone-based retinal screening has the potential to provide affordable and convenient ophthalmic care within under resourced areas. Within free clinics, its use could confer benefits in triaging who needs more immediate care. Research has looked at the ability of this technology to record the optic nerve and the potential of using this screening to diagnose glaucoma. A preliminary grading study done on a cohort of 20 patients, 15 of which reported no preexisting pathology, and 5 of which reported a previous glaucoma diagnosis yielded optimistic results. Screens were presented to graders, who assessed them on their ability to visualize the optic nerve, the clarity of the footage, and their ability to discern any pathology. The optic nerve could be visualized in 93% of cases for healthy eyes and 80% of cases for glaucomatous eyes (with significant inter-rater reliability). Graders assessed the cup-to-disk ratio of the optic nerves and reported the likelihood that they would refer each patient to additional care. These findings yielded a statistically significant difference in the measured cup-to-disk ratios of glaucomatous eyes when compared to healthy eyes as well as a significant difference in how likely graders would be to refer the patient to additional care.

Feasibility and Acceptability of using a Standalone Distraction-Based Virtual Reality Headset to Reduce Perceived Pain and Anxiety in Patients Seen in the Pediatric Emergency Department

Anshul Daga, Ajay Mittal, Jonathan Wakim, Dr. Tung Wynn
Pediatrics

In the pediatric emergency department (PED), suturing is a recurrent procedure considered to be painful and anxiogenic. Pharmacologic pain management and/or topical anesthetic creams are used to relieve pain, but distraction-based methods can also modify the painful experience and discomfort associated with suturing. Recent studies have supported that distraction is helpful in diminishing patients' ability to show concerns on the painful sensory input and as a result improve patient's experience. Virtual Reality (VR) is an emerging technology that provides an immersive user experience and has the capacity to distract patients from the negative or painful experience of procedures, which includes suturing. Given the possible short-term and long-term outcomes of poorly managed pain and suffering among children, healthcare professionals are challenged to improve patient well-being during medically essential procedures. The purpose of this pilot project is to assess the feasibility and acceptability of a standalone virtual reality headset as a distraction-based intervention for pain management in a pediatric hospital setting, specifically in patients undergoing suturing procedures in the PED.

Longitudinal Impedance of Epidural Microelectrodes Implanted in Cervical Spinal Cord

Marissa Nash, Ian Malone, Kevin Otto, Erica Dale
Physiology and Functional Genomics

The foreign body response (FBR) to implanted microelectrodes leads to an increase in impedance magnitude due, in part, to encapsulation at the tissue interface (Williams et al., 2007). In extensive cases, the Nyquist space exhibits a semi-circular arc at high frequencies indicating a parallel resistor-capacitor network due to the high density of reactive cells near the electrode. This phenomenon has many implications for in vivo research as increases in impedance can reduce efficacy of stimulation paradigms. To investigate this phenomenon in the context of epidural spinal cord stimulation, we tested the hypothesis that electrodes in close proximity to an injury site experience a more severe FBR. Longitudinal electrochemical impedance spectroscopy was performed, via Autolab potentiostat, on bilateral epidural electrodes implanted at the cervical (C4) level in rats with and without C2 spinal cord hemisection (n=8). Impedance data from day one and day five post-implant are presented here. Initial findings demonstrate that electrodes in close proximity to the injury site experience a greater increase in impedance magnitude versus electrodes farther away. Future work will look to expand the sample size and to correlate impedance changes with histological analysis of reactive cells in the area.

The Choroid Plexus and NPSLE: A Comparison of Volumetric Masking Methods
Sierra Klein, Kang-Ik Cho, Martha Shenton
Psychiatry at Harvard Medical School

In Neuropsychiatric Systemic Lupus Erythematosus (NPSLE), the 'immune-privileged' status of the Central Nervous System is breached, leading to neurological and psychological manifestations of SLE. The pathogenesis of neuropathic antibodies into the Central Nervous System is unknown. One neuroimmune interface thought to be breached is the choroid plexus. A larger choroid plexus volume could correlate with a breached blood-CSF barrier. The current study focuses on determining if the FreeSurfer algorithm is an accurate measurement of choroid plexus volume on T1 MRI images for NPSLE, SLE, and healthy controls. Since the choroid plexus is a secretory epithelial structure spread throughout the ventricles, it is difficult to locate. It is crucial that measurements are accurate to determine if the relationship between the choroid plexus and NPSLE is due to an algorithm error or a biological relationship. Using 3D slicer, the volume of the choroid plexus was manually masked and statistically compared to the volume generated via the FreeSurfer algorithm. The difference in volume generated using manual masking in comparison to the FreeSurfer algorithm was highly significant. These results call into question the accuracy of the FreeSurfer algorithm in other studies looking at the volume of structures in the brain.

Evaluating Variability in the Measurement of Global Longitudinal Strain with Slice Orientation

Shoba Abraham, Shruti Siva Kumar, Dr. Walter O'Dell
Radiation Oncology

There are many clinical scenarios in which early detection of changes in the heart's functionality can be critical in determining whether to maintain or modify a patient's treatment plan. The goal of this project was to conduct a rigorous analysis of the limitations associated with a new metric coined Global Longitudinal Strain (GLS) with regards to selection of the long-axis slice orientation. High resolution magnetic resonance imaging (MRI) scans of an isolated canine heart undergoing passive inflation were acquired. Twelve long-axis views were prescribed radially about the LV central axis. In each view, points were placed along the inner contour of the LV to create an arc from the mitral valve to the apex of the LV and then back up. The percent difference in the arc length from systole and diastole was calculated to produce a GLS estimate for each view. The GLS values ranged from 0.42 to 10.42 over the 12 views. We were able to show that there is an interpatient variability associated with the GLS metric computation. With every degree deviation from 90, which is correlated with the commonly used four chamber view, a 2 percent uncertainty in GLS is added.

Bioanalytical Method Development and Pharmacokinetics of MCI-92

Raluca Popa, Shyam Kamble, Tamara King, Erin Berthold, Abhisheak Sharma
Pharmaceutics

An ultra-performance liquid chromatography tandem mass spectrometry (UPLC-MS/MS) method was developed and validated for the quantification of MCI-92, a sigma receptor ligand, in plasma and brain homogenate samples. MCI-147, a structurally similar compound of the same class, was used as internal standard. An Acquity UPLC BEH C18 column (1.7 µm, 2.1mm×50 mm) was used for the chromatographic separation. The mobile phase consisted of 0.1% v/v formic acid in water (A) and acetonitrile (B) with gradient elution. The method had a run time of 3.2 minutes and a linearity range of 1-200 ng/mL. Multiple reaction monitoring in the positive ionization mode was used for the mass spectrometric detection, using m/z transitions 369 > 126 for MCI-92 and 448 > 350 for the IS. The method was used to analyze samples from a pharmacokinetic study in which a single dose of 2.5 mg/kg MCI-92 was given intravenously to CD-1 mice. The compound showed a high volume of distribution and moderate clearance. Additionally, the concentration of MCI-92 was consistently higher in the brain relative to plasma, indicating that the compound can cross the blood brain barrier.

Effect of Bone Morphogenic Protein Receptor Type 2 Knockdown on TGF-β Driven Fibroblast-to-Myofibroblast Transition

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Pulmonary arterial hypertension (PAH) is a disease of unknown origins that is characterized by high blood pressure in the lungs. This pressure increase can be caused by an obstruction in the small arteries, vasoconstriction, or vascular stiffness. The bone morphogenic protein receptor type 2 (BMPR2) mutation is most commonly found in patients with heritable PAH and could prove to be a therapeutic target. We hypothesized silencing the BMPR2 gene would result in a profibrotic state and promote fibroblast-to-myofibroblast transition (FMT). This was tested using WI38 human lung fibroblast cells. The cells were treated with transforming growth factor beta (TGF- β), tumor necrosis factor alpha (TNF-α), or a combination of both to stimulate cell stress fiber production. Stress fibers are cytoskeleton structures composed of cross-linked actin filament bundles which in high numbers can be an indicator of a cell in a profibrotic state. Next, we knocked down the BMPR2 gene and then stimulated our cells with TGF- β. Overall, our results suggest knocking down the BMPR2 gene will lead to more rapid expression of markers of FMT. Further work will need to be done to determine if the receptor is an efficient target for therapy but these preliminary results seem promising.

Leukoaraiosis and Mental Set During Number Placement in Clock Drawing

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Increasing leukoaraiosis (LA) contributes to difficulties in sustaining mental sets necessary for successful test completion (Lamar et al., 2001). We examined the neuropsychological command digit clock drawing condition (dCDT) mental sets regarding number placement accuracy within quadrants, testing whether higher LA volumes are negatively associated with accuracy in later quadrants.

Adults aged ≥60 years completed the dCDT and 3Tesla brain MRI. dCDT's were divided into quadrants using axes generated by specifically-designed software. Quadrants were numbered by participant's start quadrant. LA volumes were acquired via 3D fluid-attenuated inversion recovery (FLAIR) sequence and LA volumes were created by the UBO detector (Jiang et al. 2018).

Participants (n=148,M age=68.97±6.44,53% female, education=15.68±2.74). Partial correlations controlling for age and TICV examined if LA contributed to quadrant accuracy. We found higher LA associated with reduced number placement accuracy only in the third (r=-.283,p=.001) and fourth (r=-.231,p=.006) quadrants.

Our findings suggest mental set can be applied to clock drawing number placement. Within our sample, individuals' placement accuracy decreased in third and fourth quadrants. These results are analogous to negative slopes found in letter-fluency tests (Lamar, Price, et al. 2002).

Determining the effects of the antidepressant venlafaxine on locomotive responses of larval zebrafish and fathead minnows

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Antidepressants have been found in surface water despite passing through wastewater treatment facilities due to incomplete removal. The antidepressant venlafaxine has been measured at µg/L concentrations after passing through wastewater treatment facilities which necessitates the need for assessment of aquatic toxicity of this chemical. Because venlafaxine was designed to alter behavior in humans, these chemicals are likely to impact behavior in aquatic organisms. The objective of this study was to determine the effects of venlafaxine on fathead minnow and zebrafish behavior using a locomotor assay. For this assay, embryos of zebrafish and fathead minnows were exposed to a range of concentrations of venlafaxine (ng/L to µg/L) for 7 days. The larvae's locomotor response to light stimuli was measured in a white light cycle using DanioVision motion tracking system. The results indicate that Venlafaxine decreases normal locomotor response of larval zebrafish in a dose dependent manner. For fathead minnows, venlafaxine does not appear to impact the locomotor response of larval fathead minnows. These results indicate that Venlafaxine can potentially affect the behavior of fish, and therefore should be treated for in wastewater. Additionally, the sensitivity of multiple species should be considered when testing the behavioral effects of pharmaceuticals.

Growth of a Shigella flexneri Iron Transporter Double Mutant is Restored by Complementation with the Chlamydia trachomatis Putative Iron Transporter Operon

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Environmental and Global Health

Chlamydia trachomatis is a Gram-negative, obligate intracellular bacterium that causes genital tract infections in humans. While all organisms require iron, the mechanisms of iron uptake in Chlamydia are not well understood. Previously published data demonstrated that the protein Ctl0323 binds iron in vitro and that the ctl0323 gene is part of a five-gene operon (ctl0323-0327). However, this operon has not yet been characterized as an iron transporter. Iron transport systems of Gram-negative bacteria such as Shigella flexneri have been characterized, and include the Feo, Iuc, and Sit systems. We compared known bacterial iron transport systems to Ctl0323-0327 using bioinformatics and observed similarities with the S. flexneri Sit system. We therefore hypothesize that Ctl0323-0326 comprise an iron transport system in C. trachomatis. To test this hypothesis, we transformed an iron transport deficient double mutant of S. flexneri (BS934) with the inducible shuttle vector pREF100 containing ctl0323-0326 and assessed growth by measuring optical density at 600 nm (OD600) and plating for viable counts. Compared to BS934 transformed with the empty vector, which demonstrated a growth defect in liquid culture, BS934-pREF100:ctl0323-0326 demonstrated improved growth equal to the wild-type Shigella strain, 2457T-pREF100. We conclude that Ctl0323-0326 function as an iron transporter for C. trachomatis.

Observing changes in physical fitness following overfeeding and exposure to diethyl-hexyl phthalate in Danio rerio

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With the prevalence of obesity on the rise, researchers have begun to examine risk factors beyond lack of exercise and overeating. Obesogens, environmental chemical contaminants that alter standard molecular processes and promote the obese phenotype, have arisen as potential risk factors. Phthalates, a class of commonly used plasticizers, are suspected to act as obesogens, although the mechanisms by which phthalates, such as diethyl-hexyl phthalate (DEHP), exacerbate obesity are unclear. We hypothesize that DEHP in addition to overfeeding can alter blood triglyceride content and decrease physical fitness. Danio rerio (zebrafish) were randomly assigned to one of four treatment groups: Regular, Overfed, Regular + DEHP, or Overfed + DEHP. After 24 weeks, zebrafish underwent a swim tunnel test followed by euthanization, measurement, and tissue harvesting. There were no alterations in gene expression or blood triglyceride content between treatment groups, but there were alterations in gene expression and blood triglycerides following the swim tunnel assay. The Overfed + DEHP group did have a decreased critical swimming speed compared to the Regular and Regular + DEHP groups. Overall, results indicate that DEHP in conjunction with overfeeding does not significantly decrease physical fitness.

Early Performance of Hospital Value-Based Purchasing Program in Medicare: a Systematic Review

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Public Health

Over the past decade, the U.S. health system gradually moved from fee-for-service payments based on the volume of healthcare to "fee-for-value" payments based on healthcare quality. In light of the development of additional value-based programs, we performed a review and summarized studies that evaluated the Hospital Value-Based Purchasing (HVBP) program's impact on clinical processes, patient satisfaction, costs and outcomes, or assessed hospital characteristics associated with performance on the program. Overall, most studies report no impact on processes or patient outcomes with no studies assessing costs. Safety-net hospitals reportedly performed worse on several quality and cost measures, but other hospital characteristics' association with performance were unclear. This suggests that more rigorous and comprehensive risk adjustment is needed for more valid hospital comparisons. Most risk adjustment methods focus on disease severity and comorbidities, and fail to account for social determinants of health. Weighting the performance domains differently could help alleviate this problem.

Investigation of Melioidosis Outbreak in Pig Farms in Southern Thailand

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Melioidosis, caused by the Gram-negative bacterium Burkholderia pseudomallei, is a potentially life-threatening infection that can affect humans and a multitude of animals in the tropics. In December 2017, a swine melioidosis outbreak was discovered during a meat inspection at a privately owned slaughterhouse in Nakhon Si Thammarat Province in southern Thailand. The outbreak, which continued for several months, caused a dispute about where the infection began. As a result, an environmental investigation into two farms—both involved in raising the first infected pig—ensued. Through genetic sequence type comparison, the investigation revealed that a contaminated water supply at one farm was the probable source of infection. The two local sequence types identified in the infection were types 51 and 392.

Effects of Heat Stress on Shoot Apical Meristem Development

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Within the context of climate change, understanding the effects of heat stress on plant development is critical to mitigating negative impacts on crops. An important facet of plant development under heat stress is the development of the shoot apical meristem. The shoot apical meristem is responsible for the growth of the shoot, including reproductive organs. According to field observations, heat stress hastens flower development. However, it is unknown if the effect of heat stress on the shoot apical meristem is responsible for these effects. We hypothesized that heat stress would promote the flowering stage in shoot apical meristems (SAM). Tomato (Solanum lycopersicum) was used due to its status as a model organism. Tomato seedlings were placed under heat stress or optimum temperature conditions at the early vegetative stage of SAM, and they were imaged as they progressed through the stages of SAM development. Heat stressed plants exhibited slower growth and delayed development, reaching a reproductive stage much later than non-heat stressed plants. This means that heat stress delays SAM development in Solanum lycopersicum, and the early development of the SAM is not responsible for observed early flowering under heat stress.

Investigating the Digestion and Absorption of Macronutrients, and Mechanisms of Nutritional Sensing in the Gastrointestinal Tract

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Obesity is a growing world-wide epidemic. One possible mechanism contributing to obesity is the post-prandial release of gastrointestinal peptide-gut hormones, namely peptide YY (PYY) and glucagon-like peptide-1 (GLP-1), which communicate with appetite regulating centers to induce satiety. Existing evidence shows that changes in diet and nutrients alter the release of these peptide hormones. Thus, elucidating the gut hormone response is important to understanding the role of the GI tract in energy homeostasis and obesity.

In a single-blinded, cross-over design human clinical trial, we assessed the response of healthy and obese individuals to meals of different macronutrient content (high in either carbohydrate, protein or fat) over a 4-day study visit feeding period. Novel CORTRAK gastrointestinal nasal tubes, were used to collect in-vivo stomach and duodenal samples to assess gut hormone metabolite profiles in response to the meals. Blood and VAS questionnaire data were collected to determine differences in metabolite gut hormone levels and feelings of satiety. We hypothesize that the digestion of different macronutrients will yield different metabolites, gut hormone profiles and feelings of fullness in healthy and obese individuals. By understanding these variations, best practice diet modifications can be made to induce satiety and promote appetite regulation in obese individuals.

Contribution of Cells Derived from the Neural Crest in Spinal Cord Injury

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Strategies to improve spinal cord regeneration represent a potential way to improve the overall condition of patients with spinal cord injury. Axon regrowth after spinal cord contusion was previously found to be facilitated by Schwann-like cells (SLCs) which act as scaffolds for the regrowing cortical-motor neurons axons. The purpose of this project was to investigate the cellular origin of SLCs, which may be from neural crest-derived pericytes. Mice genetically engineered for GLASTCreERT2; Rosa26Tom , as well as wild type mice, received a spinal cord injury. The effect of the transplantation of multipotent mesenchymal stromal cells, previously transduced to exogenously expressing insulin-like growth factor-1 (MSC+IGF1), on the recruitment of SLCs to the site of spinal cord injury was evaluated. Based on the open field behavioral test, the transplantation of MSC+IGF1 may have accelerated recovery in movement. Furthermore, histological studies showed an increased number of cells derived from the neural crest in the areas surrounding the injury site. While the results of this experiment should be confirmed in future experiments, this project represents a step towards understanding the therapeutic potential of neural crest cells in spinal cord injury.

Faraday Instability

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Chemical Engineering

Faraday instability deals with interfacial patterns that suddenly manifest when two or more stacked fluid layers are shaken periodically in a direction perpendicular to their common interface(s), i.e. parallel to the gravity vector. When shaken at a specific frequency, there is a precise amplitude threshold above which predictable interfacial waveforms appear. Below this critical amplitude threshold, the interface is motionless and stable to small perturbations. The occurrence of patterns is due to resonance between the imposed frequency and one of the system's natural frequencies – dictated by fluid properties and the geometry of the fluid container. This project analyzes the effect of pre-patterned bounding walls on the stability of the interface by comparing experimental data with theoretical predictions obtained using a linear stability model.

BASE: A Robust User-Friendly Tool for Bayesian Analysis of Allelic Imbalance

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Allelic imbalance (AI) occurs when genetic variation in cis between the two alleles affects the regulation of mRNA expression and results in differing amounts of mRNA. The first statistical tool to identify AI differences between two "environmental" conditions was published by Novelo et. al (2014). It used a novel Bayesian statistical model, which formally tests allelic imbalance between environmental conditions while accounting for genomic context and bias in read mapping. However, there are numerous complex steps leading up to the deployment of the model that require individual execution, a time-consuming process that made it largely inaccessible. We have translated these individual steps into a robust process in Galaxy (Afgan 2018). Galaxy is a straightforward web interface that can be accessed as a part of NSF funded Cyverse or installed locally on a Linux server or workstation. The entire platform is open source and all segments of our workflow are wrapped in it. The workflow minimizes the amount of time, memory, and room for human error to increase reproducibility. Extensive testing has proved this pipeline a robust and a viable option for analyzing thousands of fastq files in a single action to identify AI in a diploid genome given many conditions.

T-cell receptor repertoires in peripheral blood encode type 1 diabetes status

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Pathology

The progressive destruction of pancreatic islet β-cells that occurs in type 1 diabetes (T1D) is mediated by a coordinated adaptive immune response. Autoreactive T and B cells have been detected within islets and the emergence of multiple β-cell directed autoantibodies are highly predictive of disease progression. Despite robust serological biomarkers, no biomarkers exist that can monitor autoreactive T cells. We hypothesized that the T-cell receptor (TCR) repertoire may contain sufficient information to foretell disease risk. To test this hypothesis, we sequenced the PBMC TCRβ repertoire of 1600 individuals from a cross-sectional cohort. We were able to roughly separate disease status by using hierarchical clustering on clonal overlap between TCR repertoires in samples based on Morisita index and TCR diversity profiles. These findings suggested that T1D patients share common TCR-encoded signatures on both clonal expansion and clonal sequences. Notably, previously published clones reactive to T1D-antigens were present with equal incidence in the PBMC samples across T1D and control groups. Our preliminary findings suggest that PBMC CDR3β signatures exist that distinguish between T1D and healthy controls. Most interestingly, without feature selection, clonal overlap and clonal expansion statistics are able to distinguish autoimmunity thereby underlining the potential disease-discriminatory role of public TCR sequences.

W-Band ENDOR EPR Of C13-Labeled Small Molecule Binding to Oxalate Decarboxylase

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Chemistry

Through X-ray crystallography and activity assays, it has been found that the manganese-dependent enzyme Oxalate Decarboxylase (OxDC) binds carboxylates in the absence of substrate, oxalate. Using carbon-13 (C13) labeling, Electron Nuclear Double Resonance (ENDOR) Spectroscopy can be used to determine bond distances between these small molecules and the active site Mn of wild-type (WT) and mutant OxDC. Resolving details of binding may illuminate factors critical to OxDC's enzymatic mechanism.

In collaboration with Dr. Robert Bittl's lab at the Freie Universität Berlin, the ENDOR spectrum of WT and the double mutant E280QC383A OxDC was investigated in W-band. The protein was poised at high pH and C13-labeled bicarbonate, oxalate, formate, and acetate were used to probe binding. Surprisingly, neither WT nor the mutant displayed a carbon-13 signal in the presence of any labeled small molecules despite experiments in the X and Q-band having shown strong C13–Mn coupling under similar conditions. A model system containing C13-labeled bicarbonate in aqueous $MnCl_2$ yielded a strong C13 ENDOR peak, indicating that the instrument was sensitive enough for the experiment. We are currently exploring at lower fields how sample preparation affects signal and plan to return to W-band once a reliable protocol is established.