4th Annual
CSU Summer Symposium
at UCLA

August 12, 2019
1:00 - 3:00 p.m.
Geffen Hall Learning Studio
We would like to thank the following for their generous support of the CSU Summer Symposium at UCLA:

CSU SUMMER SYMPOSIUM AT UCLA
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Photos and video footage taken by UCLA during the CSU Summer Symposium may be used for promotional purposes on behalf of the university.
Welcome to the fourth annual CSU Summer Symposium and Graduate Program Fair at UCLA!

We are happy to have you join us for an afternoon featuring research presentations by students from neighboring CSU campuses, and information sessions on graduate training opportunities in STEM at UCLA. The aim of the Symposium and Fair is to promote scientific exchange and provide information on graduate educational opportunities as a way to strengthen interactions between CSU capstone research programs and UCLA graduate programs.

UCLA offers a wide variety of exceptional graduate programs in STEM. The college, with Divisions of Life and Physical Sciences, is located on a single campus with the School of Medicine and hospital. This proximity provides a wealth of research training opportunities and promotes a collaborative and collegial culture of discovery and innovation that crosses traditional academic boundaries and spans disciplines, departments and schools. Our UCLA STEM community is built on core values of openness, inclusion, and respect that foster creativity and excellence by embracing a diversity of backgrounds, experience, ideas, and approaches.

We welcome CSU participants and extend thanks to our UCLA graduate program representatives.

Gregory S. Payne, Ph.D.
Director, Graduate Programs in Bioscience
Associate Dean of Bioscience Graduate Education, David Geffen
School of Medicine
Associate Dean of Graduate Education, College of Life Sciences

CSU SUMMER SYMPOSIUM AT UCLA
Schedule of the Day

1:00 – 1:20 Welcome

1:20 – 3:00 Graduate Program Tabling

2:00 – 3:00 Tabling continued with concurrent CSU Poster Session

Poster session will highlight CSU students planning to apply to UCLA who are participating in broadening participation capstone research programs such as MARC, IMSD, MBRS Rise, HMMI and others.

Light refreshments will be served.
1 Evaluating The Metabolite Profile of HER2-positive Breast Cancer Cells

SARAH ABUELREICH, Nicole Leon, Daisy Medina, Malika Sahni, Krish Krishnan, Jason Bush

CSU Fresno

One in eight U.S. women will develop breast cancer over the course of their life (American Cancer Society, 2019). It is estimated that 15-20% of breast cancer patients have overexpression of the oncogenic receptor Human Epidermal Growth Factor Receptor 2 (HER2). Overexpression of HER2 is associated with poor survival due to its aggressive growth and increased disease recurrence. Although HER2 treatments are currently available, some patients develop resistance to the treatment after multiple exposures to the anti-HER2 therapies. Our understanding of the biochemical impact of HER2 on cancer cell metabolism is poor. Our goal is to better understand the molecular mechanism of HER2 in breast cancer and identify new strategies to target the disease. By establishing the comprehensive metabolic changes, we can develop biomarkers that will allow for a more accurate selection of patients who can benefit from anti-HER2 therapies. For this project, we have a panel of eight different breast cancer cell lines with a low, medium, and high HER2 expression. We evaluated the HER2 expression using western blot and analyzed metabolites using high-resolution NMR spectroscopy. This approach allows for a better understanding of the global metabolic changes associated with HER2-positivity such that we have identified branched chain amino acid catabolism as an alternative metabolic route used by cancer cells to make the necessary building blocks that drive continued growth of cancer. The results from this research will also be used to develop a database of metabolites in this system which can be used for future data-driven research.

2 Investigating Protein-Protein Interactions in the Chp Chemosensory System of Pseudomonas aeruginosa

DIANE AGUILAR, Ramiro Patino, Joanne N. Engel

CSU Dominguez Hills, NIH MBRS RISE

Pseudomonas aeruginosa is an opportunistic bacterial pathogen that can cause severe illness and even death in patients immunocompromised. The rate of multidrug-resistance of these bacteria has increased, making it much more difficult to treat. This ubiquitous bacterium thrives in different environments since it can rapidly adapt using diverse signaling pathways, including chemosensory systems. The Chp chemosensory system is of special relevance because it controls activation of an acute virulence program upon surface contact, whose secreted toxins might protect the surface-associated bacteria from predators. The Chp system is homologous to the chemotaxis pathway in Escherichia coli, in which protein-protein interactions among its components are critical for an adequate chemotactic response. Importantly, the protein-protein interactions that take place within the Chp system are incompletely understood. Based on homology with the E. coli system, we hypothesize that the chemosensory adaptation enzymes, PilK and ChpB, directly interact with the Chp receptor PilJ. Moreover, preliminary data shows that PilJ interacts with PilH, one of the two Chp response regulators. However, it is unclear whether PilH requires phosphorylation to bind to PilJ, or if PilH can form homodimers. Using the bacterial two-hybrid system and PilH point mutants, we determined if these protein-protein interactions occur in an E. coli host. A detailed understanding of the protein-protein interactions that occur within the Chp system will provide insights on how the surface virulence program is regulated and allow further avenues for the development of new therapeutics to treat this multidrug-resistant bacteria.
Comparative Analysis of Differential Gene Expression between Elysia velutinus and Elysia Crispata

KRISHA ALGOSO, Patrick Krug
CSU Los Angeles, NSF LSAMP Bridge to the Doctorate

Sacoglossan sea slugs evolved to be photosynthetic by sharing a photosymbiosis with siphonaceous algae. This capacity varies and is demonstrated for different periods depending on the species. Certain species can digest chloroplasts completely (non-retainers), while others can ingest and store their functional chloroplasts in their digestive diverticula from a few weeks (short-term retainers) up to several months (long-term retainers). During periods of starvation, short-term and long-term retainers obtain nutrients from functional chloroplasts during photosynthesis. These differences in retention can be attributed to differential gene expression between species. Genes involved in mechanisms for lipid metabolism, stress response, and reactive oxygen species are upregulated in long-term retainers such as Elysia crispata. The same genes are downregulated in short-term retainers such as Elysia velutinus. To test this, 10 biological replicates from each species will be exposed to light-fed, dark-fed, light-starved, and dark-starved conditions two weeks. Each sample will be weighed and photographed at multiple time-points: upon preservation of the samples at the beginning of the experiment, after 10 days to two weeks, and at the end of the experiment. After two weeks of treatment, all individuals will be preserved for and extracted for mRNA to prepare a cDNA library. Transcriptomes for both Elysia velutinus and Elysia crispata will then be assembled and used to compare differentially expressed genes in both species. Comparative analysis of transcriptomes will demonstrate what allows sea slugs to differ in retention of functional chloroplasts and how animals across different phyla have evolved to show kleptoplasty.
Increased Expression of DUSP9 Increases Embryonic Stem Cell Population to Promote Breast Cancer

ALBERT J. BARRIOS, Thalia Jimenez, Alexandria Tucker, Javier Collazo, and Shehla Pervin
CSU Dominguez Hills, NIH MBRS RISE

Breast cancer is influenced by mammary cancer stem cells (MCSCs) that promote its initiation and progression. MCSC population is heterogeneous, where a subset has an embryonic stem cell (ESC) characteristics that contributes to aggressive tumor characteristics. Our lab found a correlation between reduced pERK½ levels and upregulation of DUSP9 in African American Triple Negative (AATN) breast tumors. Tumor cells and host microenvironment increased DUSP9 expression in MCSCs and ESCs. We further investigated the significance of DUSP9 expression in ESC/MCSC populations in AATN breast cancer cells. We examined expressions of DUSP9, pERK½, and ESC markers from breast cancer cells and its mammospheres by immunoblot analysis and quantitative Polymerase Chain Reaction. We observed effects of adipocytes and Oncostatin M on DUSP9 and ESC expressions. We reduced DUSP9 expression by ShRNA as well as pharmacological inhibition of all phosphatases by treatment with sodium orthovanadate, a phosphatase inhibitor. We observed that adipocytes and Oncostatin M increased DUSP9 and ESC markers expression. Mammospheres from breast cancer cell lines showed upregulation of DUSP9 and MCSC/ESC markers, which coincided with reduced levels of pERK½. Our study suggests that increased DUSP9 expression contributes to the survival of MCSC/ESC populations in aggressive AATN breast tumors. The downregulation of DUSP9 with ShRNA reduced the expression levels of DUSP9 and ESCs. Inhibition of DUSP9 with pharmacological inhibitor, sodium orthovanadate, caused increase in pERK ½ and reduced SOX2 expression. This data indicate that DUSP9 could be a target to reduce breast cancer initiation and progression.

Claudin-18 Genetic Deletion Causes Goblet Cell Metaplasia in Airway Epithelium Following Injury

NATALY J. ARIAS, Alessandra Castaldi, Zea Borok
CSU Dominguez Hills, NIH MBRS RISE

The lung is divided into the conducting airways and gas-exchange parenchymal region lined by epithelial tissue, namely airway and alveolar epithelium, respectively, each comprised of a variety of different cell types that function together to protect the lung from the external environment. Claudin-18 (Cldn18) is a lung-specific tight junction protein with the primary function of maintaining barrier integrity. Surprisingly, a Cldn18 knockout (KO) mouse model showed an increase in progenitor cell populations in both airway and alveolar epithelium. We focused here on the role of Cldn18 in the airway epithelium, and specifically aimed to determine if deletion of Cldn18 affected airway epithelium regeneration. We subjected wild-type (WT) and Cldn18 KO mice to naphthalene (NAP) injury that causes depletion of airway club cells followed by a well-characterized regeneration process. WT and Cldn18 KO mouse lungs were analyzed at day 21 post-NAP by immunofluorescence and Periodic-Schiff Acid (PAS) staining for mucus. Unexpectedly, while WT mice showed predicted regeneration with restoration of normal airway cell composition, Cldn18 KO mice developed marked goblet cell metaplasia (GCM) post-injury. Our findings suggest that genetic deletion of Cldn18 alters airway regeneration, likely regulating progenitor cell differentiation following injury. Further studies will be needed to determine the cellular origin of GCM in Cldn18 KO mice post-NAP and the role of Cldn18 in goblet cell differentiation. Deciphering the role of Cldn18 in this context may help elucidate mechanisms underlying the pathogenesis of lung diseases characterized by GCM such as chronic pulmonary disease (COPD) and asthma.
SEXISM AND ‘THE SYSTEM’: HOW GENDER IDENTITY IMPACTS THE RELATIONSHIP BETWEEN BENEVOLENT SEXISM AND THE JUSTIFICATION OR OPPOSITION OF SOCIETAL NORMS

OLIVIA T. BRUSH, KELLY A. VAN GEFFEN, CATHERINE WARREN, AMY WAX
CSU LONG BEACH

There has been a recent shift in the media to steer away from traditional gender norms. Men are discovering that being sensitive does not diminish masculinity and women are discovering that femininity goes beyond daintiness and purity. Masculine and feminine stereotypes are rooted in benevolent sexism, a subtle and sometimes undetectable form of discrimination that portrays women as weak and in need of protection from men. Benevolent sexism, masculinity, and femininity are intertwined in the context of the workplace, as advanced positions often require ‘masculine’ skills, such as leadership and assertiveness, leaving women to manage tasks dealing with empathy and communication. This is potentially because many individuals justify the way organizations and society uphold men as the dominant gender. The current study aimed to discover the relationship between benevolent sexism, masculinity and femininity, and system justification. Data collected from students at a large, public university in Southern California indicated that higher levels of benevolent sexism, when moderated by masculinity and femininity, predicted higher levels of system justification within the workplace context (n = 684, p < .01). Since there has been a push to break the confines of gender identity, the current study also examined the role of collective action. Results indicated that higher levels of benevolent sexism, when moderated by masculinity and femininity, predicts lower levels of collective action (p < .01). The current study into the impact of traditional gender norms in the workplace is important in order to see how changing gender roles will affect the workplace.

MODIFICATION OF BENZIMIDAZOLE DERIVATIVES TO INCREASE BIOSPECIFICITY

ESTEBAN BAUTISTA, DR. TAEBOEM OH
CSU NORTH RIDGE, BUILD PODER

Modified benzimidazole systems have a variety of biological activities. They act as fungicides, herbicides, and anti-parasitic agent. Most recently, benzimidazole derivatives showed to have antitumor properties and potential for use in cancer treatments. However, they cause a variety of undesired side effects. Our approach is novel in that we propose atropisomers to improve the bio-specificity of benzimidazole systems while aiming to reducing the potential for side effects. This is highly novel as it has been only recently that chemists have noticed that atropisomers plays a larger role than realized in biological systems. Due to the planarity of benzimidazole ring systems, it would be an excellent foundation to investigate this novel approach utilizing atropisomers. We present our initial synthesis approach to these systems involving functionalization of the nitrogen and incorporation of the aromatic group on the benzimidazole ring system.
10 Ionic Florescent Nanomaterial for Tumor Cell Treatment

SHALISE A BURCH, Areli Jannes Javier, Daniel Roufeil, Luis Arrioxa, Amanda Bituin, David Bwambok, Calos Luna Lopez

CSU San Marcos

The development of chemotherapeutic strategies that offer high accuracy and low toxicity to non-tumor tissues are one of the main goals of cancer research. Our project aimed to observe the effects of tunable ionic nanomaterials as novel chemotherapeutic agents. By careful choice of anions paired with rhodamine 6G it is possible to generate nanoparticles with selective toxicity towards tumor cells. Additionally, the choice of anions paired with rhodamine 6G cation have shown to influence the uptake of these nanoparticles into specific cell organelles such as mitochondria. Our first objective was to design ionic nanomaterial with different chemical and fluorescent properties and test their diagnostic and anti-cancer properties. Rhodamine 6G-based ionic salts were prepared using an anion exchange approach and cultured with cancer and stem cells (SC) at various concentration over 72hr. Nanoparticles internalized in mitochondria and were found to be toxic toward cancer cell and nontoxic toward SC. Next, we sought to explore a unique way to deliver ionic nanomaterials by taking advantage of the already present mitochondrial transfer between SCs and cancer cells. In a 2D system we show SCs can deliver mitochondria fluorescently labeled by rhodamine 6G-based ionic nanoparticles into co-cultured HEK293 tumorigenic cells. Our next step is to measure the rate and tumor toxicity of nanomaterials after transfer using a viability assay. The combined used of: i) SCs for transferring material to tumors and ii) ionic chemotherapeutic nanomaterials can open a novel area of cancer and SC research that could lead to unexplored diagnostic and therapeutic applications.
11 Can Google Cardboard's Virtual Reality Platform aid in Learning and Memory?

RYAN G. BUTLER and Dr. Larry D. Rosen
CSU Dominguez Hills

This ongoing study is examining the possibility of Virtual Reality (VR) as a learning tool. Previous research has supported the effectiveness of video games, videos, and virtual reality in learning. Google Cardboard is used to test VR as this platform as it was found to be an accessible, cost-effective form of VR. The chosen application, The People's House, is a guided tour of the White House. Half the participants view this tour through the VR application and the other half read a paper transcript. Prior to their respective experiences, VR participants are given a brief 10-minute introduction to virtual reality by playing the Google Cardboard tutorial under the supervision of an investigator. All participants are then tested on memory for presented information. Participants are then asked their opinion via survey of the medium they viewed as well as demographic information and the Media and Technology Use and Attitudes Scale (MTUAS; Rosen et al. 2013). Quiz results and opinions regarding their respective learning experiences are analyzed using demographics and the MTUAS as potential covariates. Participants are expected to number 40, with 15 participants completing the study so far. Preliminary two-tailed t-test results indicate significantly higher enjoyment (p = 0.021) for VR, higher sense of immersion for VR (p = 0.003), and that participants would recommend VR to others (p = 0.013). There is also no significant difference between quiz scores so far. Results of the study will possibly indicate which groups could benefit the most from virtual reality education.

12 Use of Triangulation in Examining Low Income Mothers Family Support For Physical Activity

BRIANNA CAICEDO and Guido Urizar
CSU Long Beach, NIH BUILD

Low-income mothers are at greatest risk for low levels of physical activity due to time constraints and responsibilities surrounding child and family obligations. Although previous research has revealed higher levels of social support to be associated with higher levels of physical activity, low-income mothers do not seem to be reaping the benefits of such support. Unfortunately, few studies have analyzed the role of immediate family in low-income mothers’ level of physical activity. The purpose of the current convergent mixed methods study was to explore the role in which family influenced physical activity among 30 low-income mothers participating in a three-month exercise program. Triangulation was used to analyze quantitative data from self-report questionnaires (i.e. Social Support for Exercise Survey), and qualitative data from focus groups and Photo Voice (i.e., mothers asked to take pictures of barriers and motivators to exercise) to identify themes on how family was associated with mothers engagement in exercise. A paired samples t-test of SSFE scores from baseline compared to three months post-intervention yielded no significant difference in levels of perceived social support (t(19) = .387, p = .703). However, themes surrounding “change,” in particular support of spouse, acted as a prominent theme throughout focus group interviews. Furthermore, mothers’ Photo Voice data revealed that children were discussed as both motivators and barriers to exercise. Additional studies are needed to examine how the role of the immediate family can be successfully integrated in physical activity interventions in order for mothers to benefit from an established support system.
13 Investigating the Neuroprotective Properties of Withania somnifera in LPS-induced Oxidative Stress in Rat Cerebellar Cortices

FERNANDO J. CANO  Amelia Russo-Neustadt

CSU Los Angeles, NIH Bridge to the Doctorate

Oxidative stress contributes to neurodegeneration and is a precursor to Alzheimer’s Disease (AD) – a neurodegenerative disorder characterized by cognitive and memory deficits. Oxidative stress results from the accumulation of reactive oxygen species mediated by proinflammatory signal transduction pathways. Our lab has shown the botanical agent, Withania somnifera (WS), has neuroprotective properties against age-related cognitive dysfunction. To investigate if these neuroprotective properties also attenuate oxidative stress and amyloid-β deposition during acute neuroinflammation, 40 Sprague Dawley rats were divided into 4 groups: Saline-control, (WS), Lipopolysaccharide (LPS) and a WS+LPS group. WS-root powder (100 mg/kg) was administered orally for 31 days. On days 14-21, the LPS+WS group received intraperitoneal (IP) injections of the endotoxin LPS (250 µg/kg). Rats were sacrificed post a 31-day treatment period. I hypothesize that if, LPS induces oxidative stress in the cerebellum of a neuroinflammatory rat model, then amyloid-β deposition will increase. Additionally, if the neuroprotective properties of Withania somnifera enhance nuclear translocation of the Nrf2 antioxidant transcription factor, then oxidative damage and subsequent amyloid-β deposition will be mitigated in cerebellar cortices. Western blot analyses will evaluate: lipid peroxidation levels (4-HNE) – an indicator of oxidative stress, nuclear Nrf2 and Aβ deposition (4G8) levels. Results from this study will elucidate if the WS-neuroprotective properties include antioxidant defense mechanisms that decrease oxidative damage and Aβ deposition in the cerebellar cortices during acute neuroinflammation.

14 The Arabidopsis thaliana glutaredoxin AtGRX660 controls lateral root development and shoot organ size

CRAIG COWLING, Sophia Carpinelli, Miguel Rosas, Matthew Escobar

CSU San Marcos, TRIO McNair

Glutaredoxins (GRXs) are small oxidoreductase enzymes that can reduce disulfide bonds in target proteins. The genome of the model plant Arabidopsis thaliana has more than 30 GRX genes, but the biological function of most of these GRXs is unknown. We previously found that a small group of Arabidopsis GRX genes is specifically activated by nitrate, a common source of nitrogen in the soil. To better characterize the function of one of these nitrate-regulated GRXs, AtGRX660, we generated transgenic Arabidopsis plants that continuously overexpress the AtGRX660 gene. We identified three transgenic lines with highly elevated AtGRX660 mRNA levels. The transgenic lines were grown in shaking liquid culture for RNA isolation, on soil in a controlled environment growth chamber for characterization of shoot phenotypes, and on nutrient rich vertically-orientated plates for characterization of root phenotypes. These AtGRX660-overexpression lines displayed a dwarf phenotype, with significantly reduced shoot system, silique length, and seed size. In addition, root system architecture was highly altered. While primary root growth was normal in the transgenic lines, lateral roots were almost completely absent. These results suggest that AtGRX660 acts a negative regulator of plant organ growth. Our findings could have agricultural relevance in plant drought tolerance, since AtGRX660 differentially affects primary root system growth and lateral root system growth.
15 Efficacy of nebulized liposomal amphotericin B for the treatment of murine pulmonary aspergillosis

JANAM J. DAVE, Adilene S. Sandoval, Jon A. Olson, Jill P. Adler-Moore
Cal Poly Pomona

Invasive pulmonary aspergillosis (IA) results in 50-90% mortality in immunocompromised patients, indicating the need for improved therapy. We investigated an aerosol delivery system to examine its potential as a novel treatment option. AmBisome (AmBi) was nebulized (neb) into a twelve compartment chamber in which triamcinolone immunosuppressed, Swiss-Webster mice were administered various regimens of neb AmBi, intravenous (IV) AmBi or PBS after intranasal challenge with A. fumigatus (ATCC 13073). Mice (n=7/group) were monitored for survival to day +21 post-challenge. Lungs, livers, kidneys, spleens and BAL (n=5/group) were collected 24h after the last treatment and analyzed for fungal burden and AmBi concentration. Neb AmBi treatment produced the best protection with 100% survival versus 43% survival with IV AmBi and 0% survival with PBS. Neb AmBi significantly lowered lung fungal burden versus all other treatments (p<0.02), delivering on average 2.6 µg AmBi/g lung with no drug detectable in the livers and kidneys. In comparison, although lung fungal burden was greater with IV AmBi vs neb AmBi, drug was detected in lungs (7 µg/g), livers (204 µg/g), kidneys (38 µg/g) and spleens (114 µg/g) of IV AmBi mice. AmBi neb was an effective and potentially less nephrotoxic and hepatotoxic treatment for murine pulmonary aspergillosis achieving significantly lower tissue fungal burden and better survival than IV AmBi, without delivering drug to the liver or kidneys.

16 Toward (Z)-Alkene Isomerization

ESTEBAN DELGADO III, Erik Paulson, Arnold L. Rheingold, and Douglas B. Grotjahn
San Diego State University, NIH IMSD

The Grotjahn lab has developed (E)-alkene isomerization catalysts that contain cyclopentadienyl (Cp) ligands, as well as phosphine ligands. These catalysts are highly selective in the production of (E)-alkenes from terminal alkenes. We hypothesize that the high (E)-selectivity originates from the bifunctionality of the phosphine ligand. A potential approach to inducing (Z)-selectivity is to modify the Cp ligand by incorporating bulkier R groups and including a pendant base. Methodologically, we are conducting water and air free synthetic experiments to produce altered Cp ligands. These ligands are characterized by nuclear magnetic resonance and recrystallization, purified by silica gel column chromatography, and subsequently attached to ruthenium metal centers by oxidative addition under water- and air-free conditions. The consequent ruthenium complexes are tested for (Z)-alkene isomerization efficacy through iterative nuclear magnetic resonance experiments. Currently, we synthesized a small variety of Cp ligands, with one ligand being novel. In addition, we produced a novel ruthenium complex, but have not yet tested it for any (Z)-alkene isomerization efficacy. In summary, the synthesis and characterization of functionalized cyclopentadienyl ligands and a respective ruthenium complex will be presented.
17 Threatened Turtle Species in the Oak Openings Region Differ in Vulnerability to Edge Effects on Nesting Ecology

ALEXIS A. DIAZ, Sarah E. Carter, Henry Streby, and Jeanine M. Refsnider
CSU Dominguez Hills, NSF LSAMP

The Oak Openings Region contains critical habitat types supporting rare species, yet is seriously threatened by human disturbances. Two flagship Oak Openings species are the eastern box turtle (Terrapene carolina) and spotted turtle (Clemmys guttata), both of which are state-Threatened in Ohio. As habitat becomes increasingly fragmented, turtles on nesting forays are more likely to encounter anthropogenic edges, which can have adverse impacts on survival and reproductive success. We compared nest-site choice between box turtles and spotted turtles to determine whether nest success varies with distance from anthropogenic edges. We radio-tracked gravid turtles of both species throughout the nesting season and located nest sites in 2018 and 2019. We found that spotted turtles nested substantially farther than box turtles from anthropogenic edges (325 and 192 m, respectively). The overall nest predation rate for both species was only 6%, and distance from edge did not predict whether a nest was depredated. There was no difference in shade cover over nests between the two species, with both species nesting under 30-45% shade cover. In terms of nest macrohabitat, both species nested in grassland habitat rather than a closed habitat or wetland. Our results suggest that spotted turtles may more strongly favor core habitat for nesting than do box turtles, and thus would be more affected by habitat fragmentation. We recommend that land managers maintain core habitat patches for these vulnerable turtle species that include open areas for nesting that are at least 350 m from the nearest road or other anthropogenic edge.

18 The Influence of Telemedicine Dosage in Promoting Weight Loss in Older Patients Who Are Obese

PATRICIA DIONICIO, Michelle Alencar, Niloofar Bavarian, and Melawhy Garcia
CSU Long Beach, NIH BUILD

Telemedicine provides a potential avenue of access between physicians and older adults who are obese and face economic and physical barriers when attempting to access health services. However, few studies exist that have targeted older adults (≥ 65 years), or compared the outcomes of telemedicine obesity programs between different age groups. Thus, testing the effectiveness of a dosage response for a telemedicine-based weight loss program with health coaching in this population is warranted. The purpose of this study was to evaluate the influence of the inHealth Medical Services, Inc. Medical Weight Loss (MWL) and Chronic Care Management (CCM) program dosage on weight loss. This study also aimed to assess the influence of constructs from the Technology Acceptance Model on telemedicine dosage in patients who are obese. The proposed study incorporates two components: Study 1 will focus on the influence of dosage, while Study 2 will focus on factors that influence dosage. Preliminary findings suggest that the number of telemedicine visits within a primary care setting influences percent body weight loss. Our next steps will entail analyzing retrospective de-identified patient data as well as implementing a survey influenced by the Technology Acceptance Model. *Note: this project is a thesis in partial fulfillment of the Masters of Public Health program at California State University, Long Beach.
19 Behavioral Mechanisms Involved in Food Preference in Drosophila Melanogaster

BRIDGET K. DIVIAK, Ashley Carter
CSU Long Beach, NIH BUILD

To reveal the behavioral mechanisms involved in food preference in fruit fly Drosophila Melanogaster, oviposition choices were compared for pairs of food flavorings. Although it is known that the Drosophila relies on the presence of the yeast Saccharomyces cerevisae and acetic acid as oviposition guides, food flavor preferences are largely unknown. Furthermore, the degree to which preferences may be influenced by individual history or even via epigenetic mechanisms is unknown. We mated isogenic and identical parental generation flies and allowed them to oviposit in food flavored with various extracts and observed subsequent oviposition preferences in their offspring (individuals exposed to the flavors) and F2 generation flies (which were exposed to control food lacking the flavors). Our data showed that exposure in earlier stages of development, and even in parents’ larval environments, may modify Drosophila food preferences. These results have implications for insect population control and sympatric speciation.

20 Environmental and Geographic Differentiation in Syntrichia caninervis

UGBAD FARAH and Kirsten Fisher
CSU Los Angeles, NSF LSAMP Bridge to the Doctorate

Syntrichia is one of the most ecologically dominant groups of mosses across arid habitats in western North America, and is frequently associated with biological soil crust (biocrust) communities in the Mojave and Colorado Deserts. Within biocrust communities, the species S. caninervis serves as an excellent model system to investigate how environmental stress influences life history strategies and diversification. Previous studies have examined genetic diversity in S. caninervis populations within a limited ecological and spatial scale. This study investigates the potential for genetic differentiation of populations of S. caninervis with both environmental and physical/geographic distance. At two geographically distant sites (Sheep Mts, NV, and Colorado Plateau, UT), we sampled three S. caninervis populations along an elevation gradient (Low / Mid / High) to capture differing levels of overall environmental stress at each (geographically proximate) site. These samples, collected along well-characterized ecological gradients, and a set of S. caninervis population samples representative of the species’ geographic range in western North America, will be genotyped through RAD sequencing. These genotype data will be analyzed to determine whether genetic distance corresponds to either ecological or geographic distance between collection localities. If diversity is influenced strongly by physiological specialization within this species, we anticipate that S. caninervis sampled in high stress environments, irrespective of geographic distances, will be more similar than mosses that are in environments of low stress but physically closer.
EMMANUEL FLORES, Mo Kaze, Mark Sistrom, Tricia Van Laar

CSU Fresno, NIH Bridge to the Doctorate

Bacillus subtilis and B. coagulans are deemed “generally recognized as safe” (GRAS) by the FDA and are added to a plethora of probiotic products. Since these types of probiotics have historically shown to be therapeutic without negative side effects, the magnitude of antimicrobial resistance (AMR) and potential to transfer AMR genes has been overlooked by the food industry. In this study, we aim to determine if these probiotic strains of Bacillus are resistant to clinically relevant antibiotics. We also aim to analyze their potential to transfer AMR genes to enteropathogens. Kirby-Bauer disc diffusion assays were performed to determine if any of these probiotic Bacillus strains are resistant to clinically relevant antibiotics. In B. coagulans and B. subtilis strains, we observed resistance to ampicillin, bacitracin, clindamycin, chloramphenicol, and erythromycin. Additionally, we observed intermediate sensitivity to ampicillin, clindamycin, and rifampin. Our bioinformatics methods utilized the Comprehensive Antibiotic Resistance Database (CARD) to analyze genomes of these probiotic Bacillus strains for genes that confer AMR resistance and found genes conferring resistance to all classes of antibiotics. Lastly, conjugation assays will be performed to determine if AMR is transferred from probiotic Bacillus to enteropathogens. Pre-conjugation Kirby Bauer assays have been performed on B. cereus and Salmonella enterica to establish AMR profiles as baselines to compare with post-conjugation Kirby Bauer results to observe the transfer of AMR. Taken together, results from this study will provide insight into the potential risks of AMR in probiotic supplements and its spread to enteropathogens.

JAZMIN GARCIA, Anthony I. Squillaro, Alexa M. Fode, Laura-Marie A. Nucho, David F. Chang, Tracy C. Grikscheit

CSU San Bernardino, CIRM

The limitation of donor tissue for patients with life-threatening metabolic disorders of the liver mandates an alternative. Human induced pluripotent stem cells (iPSC) may offer the potential for a renewable source to generate hepatocyte-like cells as a possible cellular therapy. We hypothesized that human iPSC-derived hepatic progenitor cells can generate functional tissue-engineered liver (TELi) in a murine model. Human iPSC line LiPSC-GR1.1, was directly differentiated into definitive endoderm (DE) by day 4 and subsequently into hepatic progenitor cells (HPC) after 17 days of suspension culture. To generate TELi, HPC were seeded onto a biodegradable scaffold and implanted in the omentum and subcutaneous abdominal wall of NOD/SCID mice for either 6 weeks or 3 months. Day 4 DE contained an average of 23.7%±6.6 SOX17+/CXCR4+ cells. Day 17 HPC expressed hepatic markers (HNF4α, AFP, TBX, albumin), biliary markers (EpCAM, DESMIN, CK19, ECAD) and proved functionality by PAS, Oil Red O stain and the detection of bile on H&E. Both 6-weeks and 3-months TELi contained ductular structures resembling biliary epithelium on H&E and also contained CK19+ cells with the expression of albumin and hepatocyte specific antigen which co-stained with human markers indicating human origin. Secretion of human albumin by TELi (6-weeks and 3-months) in host serum was quantified by an ELISA assay. Human iPSC-derived HPC can generate functional albumin-producing short- and long-term TELi in a murine model. Further enhancement of this protocol may improve the function and efficiency of hiPSC-derived TELi for future human therapies.
23 Theoretical Study of 3FC-TZN and its Host-Guest interaction in the Determination of Stable Electroactive Materials

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Reliable theoretical 1H NMR, HOMO, and LUMO is computed for the molecular recognition (Host-Guest) and its role on redox activity, the 2,4,6-Tris(p-ferrocenylanilino)-1,3,5-triazine (3FC-Tzn) with cucurbit[n]uril that has been synthesized experimentally. The Density Functional Theory (DFT) of B3LYP/6-31G* method is used to optimize each molecule and then optimize both structures together using the DFT calculations with the M062X/6-31G* method in the solvent of DMSO. These results are used to compare the computational calculations with the experimentally synthesized Host-Guest. These theoretically calculated values are within a 5% relative error when compared to the experimentally chemical shift. The 3FC-Tzn is a star shaped molecule with three repeating units of p-Ferrocenylaniline groups connected by central triazine core. The 3FC-Tzn is used as a guest to form a Host-Guest complex with cucurbit[n]uril. The cucurbit[n]uril is a macrocyclic molecule and acts as host to form an intercalated Host-Guest complex with neutral and cationic molecule. Redox active compounds have been used in batteries, sensors, and solar cells. Many enzymes regulate their activities through redox process naturally. It has been reported several redox active compounds in the literature. Among them, Ferrocene has attracted more attention because of its low oxidation potential as well as its reversible one electron transfer process. Ferrocene is an organometallic complex with an iron (II) that is sandwiched between two stacked cyclopentadienyl rings. Having been synthesized from commercially available Ferrocene and cyanuric chloride that was characterized by different spectroscopic techniques, such as NMR, Mass Spec, IR, and UV-Vis and compared to reliable computational modeling.

24 Manipulating Electric Fields to Lyse Algae for Biofuel Applications

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Algae-derived biofuel has the potential to revolutionize fuel production methods by providing a cleaner alternative to fossil fuels. This is achieved by extracting the lipids from algae cells and transforming them into usable biofuel. To extract lipids from algae, we use Pulsed Electric Fields (PEF’s) to lyse (rupture) the cell membrane. These PEF treatments are delivered to the algae cell using an electroporator (high voltage pulse generator). The circuit charges a capacitor that discharges into the algae sample located between two parallel conductive plates. Our team developed an impedance model of the cultured algae strain, Chlorella, to design our own electroporator device to expand PEF intensity and pulse chamber capabilities beyond available models. We successfully built a circuit that subjects the algae to PEF’s to lyse it. Developing this device is the team’s first step towards having our own algae-electroporator to identify electrical pulse parameters that efficiently lyse algae cell membranes.
Tracing Unconventional Gene Arrangement Highlights the Recruitment of Independent Cellulases for Cellulose Synthesis in Bacteria

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Cellulose synthesis and subsequent degradation is an essential part of carbon cycling across many ecosystems. Beside plants, some bacteria produce cellulose as part of their biofilm. The bacterial cellulose synthesis (bcs) operon encodes the enzymes involved in this process. However to date, the detailed enzymatic mechanisms of cellulose production remain unclear. However research suggests that a cellulase is required for efficient synthesis (i.e., bcsZ). Here, we investigated the distribution and architecture of the bcs operon in sequenced bacterial genomes through genome mining. First, most bcs operons are identified in Proteobacteria, and few in Firmicutes and Spirochaetes. Next, strains with bcsABC generally contained less cellulases than other bacteria. Finally, regarding the bcsABC strains but no identified bcsZ gene, we investigated the genomic context of distantly located cellulases to determine whether they can still participate in cellulose synthesis or be involved in cellulose degradation. We identified both cellulases in potential hydrolytic and biosynthetic clusters. In the future, the sequence of the potential biosynthetic cellulases will be aligned in order to build custom HMM-profiles to differentiate the biosynthetic from hydrolytic enzymes.
Preventing Meltdowns: Performance Impacts of Patching Processor Vulnerabilities

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Meltdown is a computer security vulnerability disclosed in January 2018 which affects the vast majority of desktop, laptop, and cloud computers produced since 1995. Meltdown takes advantage of a hardware performance optimization that is normally invisible to software. However, the vulnerability allows any program to access the assumed private data of other users or even the operating system itself. This would allow an attacker to gain passwords, financial information, or even state secrets. Kernel Page Table Isolation (KPTI) is a software patch that aims to protect operating systems from Meltdown at a cost to overall system performance. We measured the performance of representative applications and identified classes of applications whose performances are particularly affected by KPTI. Using hardware performance counters we are able to correlate these performance decreases to low-level hardware events.

Wettability of Powders

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In this work different methodologies that are used to measure the wettability of powders are studied in detail. In solid pharmaceutical dosage forms, the wetting properties of both raw and processed material is one of the critical material attributes, ranging from formulation development to the design of manufacturing pathway. It has been recognized that the different manufacturing process would significantly change the wetting behavior of material. In addition, the wetting properties of raw and intermediate material directly affect the dissolution performance and bioavailability. For this reason, the characterization of wetting properties is inevitable for quality control in advanced pharmaceutical manufacturing. Several techniques have been developed to identify wettability of powders. These include the sessile droplet, capillary rise, immersion and condensation methods. The sessile drop method (i.e. drop penetration method) is the most common method. In this method a single liquid droplet is released to a powder bed and the contact angle of the liquid is then measured on the powder bed. This method is the easiest to replicate, but it is also very sensitive to powder bed condition. For instance, air may get trapped inside the powder bed. The capillary rise method is a layer of powder and the fluid is pushed up through it. In the immersion method the powder bed is placed under the liquid and the phase interaction between the solid and liquid is observed. In the condensation method the resting drops on the surface are analyzed.
**Evaluating the Efficacy of a Liposomal Aspergillus Vaccine against Pulmonary Aspergillosis in Neutropenic Female Swiss Webster Mice**

NICKOLAS HOLZNECHT, Matthew Slarve, Jon Olson, Jill P Adler-Moore

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Introduction: Pulmonary aspergillosis is a life-threatening infection in immunocompromised patients, with the highest rates of infection due to Aspergillus fumigatus. The rates of aspergillosis have been increasing as the numbers of immunocompromised individuals have increased due to use of corticosteroids and/or alkylating agents. Antifungal drug treatments with liposomal Amphotericin B (AmBisome) or azoles, such as Vfend, are helpful but only produce 50% survival. To address this, we established a cyclophosphamide immunosuppressed model of aspergillosis in female Swiss Webster mice and tested an immunotherapeutic liposomal Aspergillus protein vaccine (VesiVax, Molecular Express Inc) to determine whether or not, mice given this Vaccine, prior to immunosuppression and fungal challenge, would further enhance antifungal drug efficacy.

Methods: Mice were vaccinated d0 (subcutaneously), d21 and d42 (intranasally), immunosuppressed with cyclophosphamide and on d56 challenged intranasally with A. fumigatus (ATCC 13073). Groups of vaccinated mice were given oral Vfend 12h, 24h, 36h, 48h, 60h, 72h post challenge or no additional antifungal drug. Other groups were given just Vfend or phosphate buffer. Mice were evaluated for morbidity until d77. Results: The Vaccine, and Vaccine+ Vfend significantly protected mice against pulmonary aspergillosis as shown by decreased disease signs, increased survival (67% and 89%, respectively vs 22% for Vfend or buffer treatments alone, p < 0.05) and decreased colony forming units in the lungs of infected mice. Conclusion: While mice given Vaccine alone were protected, mice given both Vfend and the Vaccine had the best survival, and were much better protected than mice given just Vfend.

**Determining the Role of Linker Region Phosphorylation in Polypyrimidine Tract Binding Protein 2 Neuronal Splicing Regulation**

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CSU Fullerton, NIH MARC

Polypyrimidine Tract Binding Proteins, PTBP1 and PTBP2, belong to a family of RNA binding proteins that function to regulate alternative splicing. PTBP1 and PTBP2 can bind to CU rich elements within the premature mRNA to promote or inhibit splice site selection. PTBP1 is expressed in nearly all tissues but is absent in neurons while PTBP2 is expressed almost exclusively in neurons. Problems with alternative splicing can lead to the production of aberrant proteins and result in neurodegenerative diseases. PTBP1 and PTBP2 share 74% sequence identity and are similar in domain arrangement. These proteins regulate over-lapping and distinct sets of target exons. Notably, differences in expression patterns and splicing activity play a critical role for neuronal differentiation and maturation. How these two proteins can exert different tissue specific splicing outcomes remains unknown. Recent mass spectrometry studies have revealed that PTBP2 is phosphorylated at a greater number of residues than PTBP1 in the unstructured N-terminal and linker regions. Thus, the hypothesis underlying this study is that phosphorylation of PTBP2 N-terminal and linker regions dictates its neuronal specific splicing activity. To test this, we have generated PTBP1-PTBP2 chimeras. The constructs were tested for protein expression in mouse neuro 2A cells via Western Blot. Our results highlight the chimeras are well expressed. We are currently investigating their splicing activity using a reporter minigene that contains a test exon differentially regulated by PTBP1 and PTBP2. The results from this study will determine the role of the N-terminal and linker regions in PTBP2 neuronal splicing regulation.
Controlling the Localization of Cell-Fate Determinants via Micropatterning Method

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Stem-cells are non-specialized cells that are unique for their ability to differentiate into specialized cells. We are able to differentiate human adipose derived stem cells to several cell lineages and types, including osteoblasts and chondrocytes. However, the rate of differentiation remains a slow and inefficient process that limits our scale up capabilities. Thus, understanding how to precisely regulate cell fate remains a key goal in stem cell and musculoskeletal research. A driving force of stem cell differentiation is the asymmetrical localization of cell-fate determinant factors. In our project we focused on the cell-fate determinant Numb, commonly known for inhibiting the Notch Signaling Pathway, responsible for regulating differentiation. We sought to regulate Numb localization by controlling cell morphology and spreading. To do this, we used a micropatterning method that can aid in controlling the regulation of stem cell morphology. We approached this by plating cells on different micropatterned slides aimed to produce different shapes: circles, squares, and triangles. We cultured human adipose derived stem cells (HAD-SCs) for 3 days and used Fibronectin to promote cell adhesion. As a result, the Numb was highly localized in areas of the cells that appear to be actively spreading. Numb localization depended more on the cell being actively spreading than in a specific morphology. Numb was localized in regions of the cell closer to the substrate rather than the top of the cell. These results indicate that Numb localization is a dynamic dependent process that depends on cell-substrate interactions.

The Effect of Lovastatin on Processing of Activating Transcription Factor 6

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The Endoplasmic Reticulum (ER) is the largest eukaryotic organelle which is known to mediate multiple integral cellular processes such as protein synthesis, folding, and trafficking. Perturbation of these processes leads to accumulation of misfolded proteins within the ER lumen and a type of cellular stress known as ER stress. Upon the induction of ER stress, cells activate the Unfolded Protein Response (UPR), an evolutionarily conserved transcriptional program, to restore ER homeostasis. The UPR is regulated by three transmembrane sensors, one of which is Activating Transcription Factor 6 (ATF6). During ER stress, ATF6 translocated to the Golgi and undergoes proteolytic cleavage by Golgi-resident proteases to release its N-terminus to move to the nucleus. The same proteases cleave Sterol Regulatory Element Binding Proteins (SREBPs) in a manner similar to ATF6 in order to regulate lipid homeostasis. Previous studies have shown that the cleavage of SREBPs is promoted by Lovastatin, a common drug prescribed to lower blood cholesterol levels. We hypothesized that Lovastatin should also induce cleavage of ATF6 in a manner similar to SREBPs triggering the UPR. Our preliminary data collected using HeLa cells as a model system suggest that Lovastatin treatment alters level of some of the key UPR proteins. Future experiments aim to further confirm the effects of Lovastatin on the UPR.
Obese, diabetic male ICR mice have delayed mortality and morbidity to H1N1 and H3N2 infection compared to non-obese, non-diabetic controls

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Diabetes appears to be a risk factor for more severe influenza infection and nearly one-third of Americans are diabetic or have pre-diabetes. Vaccination against influenza is recommended for diabetics, but the efficacy of vaccination in the context of diabetes is poorly understood. The purpose of the study described is to establish a mouse model of type 2 diabetes that can be used to characterize the efficacy of influenza vaccination in this context. Male ICR mice were fed a high fat diet until they became obese, at which point they were treated with nicotinamide (60mg/kg) prior to streptozotocin (100mg/kg) to decrease insulin production while still preserving some beta cell function. Mice became diabetic within a few days (blood glucose >200mg/dL) and serum insulin remained low compared to obese only mice, indicating type 2-like diabetes instead of type 1. Obese diabetic mice or non-obese, non-diabetic mice were challenged with H1N1 (PR8) or H3N2 (x31). Death, morbidity, and weight loss were delayed by about two days in obese diabetic mice for both influenza serotypes, but these data were not statistically significant. Future studies will be performed to determine if the diabetic mice have an attenuated non-self-destructive cytokine response to challenge or if the difference in virulence between diabetics and non-diabetics that has been observed by others can be explained by influenza strain. This murine model of diabetes will then be used to compare the protection and immune responses generated by influenza vaccines in diabetic versus non-diabetic mice.
35 The Role of Testosterone in Tree Swallow Territorial Aggression

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Aggression is important for achieving reproduction and increases survival in many free-living animals. Specific types of aggression are performed by different animals and by different sexes. Female and male tree swallows (Tachycineta bicolor) both engage in territorial aggression to successfully claim a nesting site. Decades of research support that the steroid hormone testosterone (T) is predictive of male aggression. However, the biological mechanisms underlying female territorial aggression remains uncertain, perhaps because females have lower T levels than males, and high T levels constrain egg production and maternal care. Recent work shows that other components of the androgenic-signaling system related to T, like gene expression of receptors that regulate circulating T levels throughout the body, are better predictors of female songbird territorial aggression. To further explore this in territorial tree swallows, we measured their aggressive behavior during a simulated territorial intrusion and collected their trunk blood and gonads to measure T and androgen receptor (AR) mRNA expression. Ultimately, we found that females were more actively aggressive than males, in that they attacked and closely approached a conspecific decoy more often than males. Surprisingly, female T levels were predictive of their attack frequency, but not males. Interestingly, there were no sex differences in AR mRNA expression, nor was there a relationship between T levels and AR expression levels in females or males. This hints that enzymes that convert T to other metabolites, and not circulating T alone, may be important for explaining territorial aggression in female and male tree swallows.

36 Using Hyperelastic Material Models to Investigate the Extracellular Matrix of Pancreatic and Cardiac Tissues

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Changes in the extracellular matrix (ECM) of tissues are observed in a wide array of acute and chronic diseases. These changes result in differences in the tissue biomechanics recorded during compressive testing, which would enable the development of a novel method for classifying and diagnosing disease. However, understanding how structural changes in the ECM occur and change with disease development is a challenge due to the complex viscoelastic behavior of biological samples and the limitations of current biomechanical models. To overcome these challenges, novel physical and computational models have been developed for specific tissue types and disease pathology. By taking experimental compressive testing results obtained with Optical Fiber Polarimetric Elastography (OFPE), models were developed to understand how specific structural changes in the ECM affect the complex viscoelastic behavior of biological samples. Based on physiological parameters, determined from testing and imaging of cardiac, cartilage, and pancreatic tissues, we designed simple geometric structures in SolidWorks. The structures were imported to Abaqus, a finite element analysis software, to model how geometric changes impact the viscoelastic behavior observed during compressive testing. Geometric transformations in the structure were systematically conducted to simulate the damage that occurs during disease development. After FEA modeling, structures were 3D printed using projection microstereolithography and compressively tested. The results from the computational and physical modeling demonstrate how these novel models can be used to understand the complex role of the ECM in dynamic tissue biomechanics.
Effects of Withania somnifera on tau phosphorylation after inflammation caused by lipopolysaccharide

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CSU Los Angeles, NSF LSAMP Bridge to the Doctorate

Millions of Americans suffer from neurodegenerative disorders such as Alzheimer’s disease (AD) that affect memory and lifestyle. Researches have suggested that one of the contributors in the onset of Alzheimer’s disease is mild and chronic inflammation. As a person grows older, they are more prone to inflammation. Current medical therapies such as anti-inflammatory drugs meant to reduce symptoms of Alzheimer disease symptoms, such as cognitive decline, have been unsafe and inefficient. In order to provide a safe treatment with minimum side effects, some researchers have switched their interest to Ayurvedic medicine like Withania somnifera (WS). WS has been used in Indian medicine for hundreds of years and is known to reduce inflammation and improve memory. In this research, I hypothesize that WS will reduce levels of tau phosphorylation induced by inflammation caused by lipopolysaccharide (LPS) injections. In order to investigate the question, four different groups formed by young Sprague-Dawley rats were created. The young rats received WS as part of their daily diet for thirty days and then at day fourteen they received an LPS injection in order to induce inflammation. I will measure the phosphorylation of tau protein sites Ser202/Thr205 known to be hyper phosphorylated by inflammatory stimuli via western blots. I will examine brain areas that are associated with memory and cognition such as the hippocampus and prefrontal cortex. This project will help identify potential treatment for the regulation of tau phosphorylation in Alzheimer’s disease.
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Myelin basic protein (MBP) is an intrinsically disordered protein that maintains the integrity of the myelin sheath and whose degradation is implicated in multiple sclerosis (MS). MBP is heavily modified posttranslationally including phosphorylation and methylation of serine and arginine residues respectively. Phosphorylation by various kinases is generally absent in patients with MS. Symmetrically dimethylated arginine (SDMA) as well as the enzyme that produces this modified arginine residue PRMT5, have both been implicated in MS and are established markers of autoimmunity. While each of these modifications has been studied independently, it is possible that they interfere with each other. Herein we set out to investigate whether a phosphorylated serine residue will block deposition of methyl groups by PRMT5. MBP contains a conserved CK1 phosphorylation motif (K/R-X-K/R-X-X-S/T; motif: KGRGLS) where serine is phosphorylated in the presence of a neighboring positively charged arginine group. We use this established motif to study the role of phosphorylation on neighboring arginine methylation. We hypothesize that in the presence of phosphorylation, arginine methylation will be blocked which may help explain why patients with MS, which have a decrease in phosphorylation, also have increased levels of SDMA catalyzed by PRMT5. To determine whether there is an interplay between methylation and phosphorylation in MBP, recombinant MEP/PRMT5 will be utilized for in vitro enzymatic reactions with modified (phosphorylated) and unmodified peptides based on MBP. The reactions will then be acid-hydrolyzed and detected for the formation of methylated arginine residues by reverse-phase HPLC.
Applying Machine Learning Techniques to Forecast Earthquake Probabilities on Different Sections of the San Andreas Fault System

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The San Andreas Fault System (SAFS), comprised of the San Andreas, Hayward, Elsinore, and San Jacinto faults, has been experiencing an absence of Mw >7.0 earthquakes for a period of 100 or more years. The SAFS poses a significant seismic hazard to California, resulting in increased risk to millions of residents and billions of dollars of potential damage. As part of the 2019 Undergraduate Studies in Earthquake Information Technology (UseIT) internship program, the Machine Learning (ML) team created a statistical time-dependent potential earthquake forecast for the next 30 years using deterministic earthquake simulations. The Rate-State Earthquake Simulator (RSQSim) is a physics-based fault model system that generates earthquake catalogs. The ML team filtered a 1 million year California statewide catalog produced by RSQSim using the Uniform California Earthquake Rupture Forecast version 3 (UCERF3) fault model for Mw >7.0 events, where we binned the events into 100-year training intervals and 30-year predictive intervals on 33 sections of the SAFS to train/test our model. We applied three different machine learning algorithms to forecast time-dependent earthquake probabilities — logistic regression, neural network, and random forest classifier. These models determine the marginal probability of rupture on a specified fault section given information about the state of the SAFS. We compare the different approaches using log-likelihood ratio relative to a time-independent forecast. Our results show that the random forest algorithm has an increased log-likelihood score with respect to the baseline forecast, while the logistic regression and neural network have the opposite result.

Metabolic Changes in Adipose Tissue in Response to Chronic Electronic Cigarette Exposure

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Tobacco use is a leading cause of preventable death in the United States. In recent years, electronic cigarettes (e-cigarettes) use by youth has augmented at a disturbing rate. Nicotine can induce lipolysis in adipocyte tissue, leading to increased serum free fatty acids (FFA). Chronic increase of FFA has been shown to contribute to the development of insulin resistance and metabolic syndrome. In adipocytes, decreased levels of Sirtuin 1 (SIRT1) are associated with metabolic syndrome. Our laboratory has shown that chronic e-cigarette exposure induces cardiac dysfunction, atherosclerosis and hepatic steatosis in the ApoE knockout (KO) model. In this study, we investigated the role of adipocyte tissue in the metabolic changes associated with e-cigarette exposure. We developed a mouse e-cigarette exposure model system that delivers nicotine in mice that is equivalent to that in human e-cigarette users. ApoE KO mice were exposed to saline, e-cigarette without nicotine [e-cigarette (0%)] and e-cigarette with 2.4% nicotine [e-cigarette (2.4%)] aerosol for 12 weeks. We observed increased serum FFA levels in mice treated with e-cigarette (2.4%). Western blot analyses showed that mice treated with e-cigarette (2.4%) had decrease levels of SIRT1 when compared to with control mice. The increased levels of serum FFA and SIRT1 depletion may suggest a role of adipocyte tissue in the metabolic effects produced by e-cigarettes. Understanding the consequences of e-cigarette use on metabolic disease is directly relevant to the development of policies related to e-cigarette use.
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Nanostructures, features that are generated on the scale of 1-100nm, have potential in many applications including optoelectronics, drug delivery vesicles, and sensors.1 Mixed polymer brushes, polymer brushes composed of two or more unique polymer types, have been shown to give rise to distinct nanostructures by tuning the ratios of the polymers.2 Polymer brushes, polymers that are covalently tethered to a solid surface of any geometry, are mechanically and chemically robust, but their thermal stability is not well understood.3,4 Because many potential applications involving polymer brushes require elevated temperatures, understanding and tuning the thermal stability of polymer brushes is important.5 We are studying the thermal properties of homo, binary, and ternary polymer brushes consisting of polystyrene, poly(methyl methacrylate), poly(4-vinyl pyridine), and poly(2-vinyl pyridine). The polymer brushes are synthesized using free radical polymerization and the thickness of the brushes is measured with spectral reflectance (SR). By examining brush density, brush thickness, and molecular weight information we have a better understanding of whether the number of unique polymers in a polymer brush or the polymer identity determines the thermal stability.

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Amyotrophic Lateral Sclerosis-Parkinsonism Dementia Complex (ALS-PDC) has been affecting a lot of people in Guam community. Many studies have linked Beta-Methylamino-L-Alanine (BMAA), a non-protein amino acid, to the development of ALS-PDC. BMAA is produced from a cyanobacteria algae and can be further found in human food supply chain. The symptoms of ALS-PDC are described by loss of motor function, tremors, and dementia due to degradation of neuron. In bicarbonate environment, BMAA has a structure that is much alike to glutamate, this increasing the chance that BMAA can act as an agonist to the glutamate receptor N-methyl-D-aspartate (NMDA) which lead to excitotoxicity to neuron cells and further degenerate the cell. Kynurenic acid is a non-specific NMDA receptor antagonist has been shown to interfere with the activity of BMAA. The interaction of BMAA and Kynurenic acid is analyzed through the circadian rhythm activity and viability outcomes of wild-type Drosophila melanogaster. Two Drosophila Activity Monitor 2 (DAM2) system are utilized to measure the activity level of 64 individual fruit flies (Gender and Age-Match). An IR sensor is built in the monitor to analyze the activity level by the number of times the fly passes by the sensor. The experimental groups are administered with BMAA, Tryptophan, Kynurenic Acid, cofeeding Kynurenic Acid + BMAA, and the control group is administered with standard fly agar. Fly activity is monitored for 10-day period (12L/12D at 22 celcius). This project investigates the therapeutic potential of Kynurenic acid in ALS-PDC model.
TOXIN SENSITIVITY OF SEA ANEMONE SHAKER CHANNELS

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Nematostella vectensis (Starlet Sea Anemone) has provided valuable insights into the evolution of nervous system development and excitability. For example, Nematostella has all types of voltage-gated K+ channels (Kv) found in higher animals, demonstrating that these critical regulators of neuronal excitability evolved prior to the divergence of cnidarians and bilaterians roughly 600 million years ago. It is also well known that anthozoans such as Nematostella contain diverse voltage gated potassium channel (Kv) toxins in venoms that they use to paralyze prey or defend themselves in their natural habitats. This raises the question of whether anthozoans have developed resistance to their own toxins at the level of the channel targets themselves. To test this, we are examining whether Nematostella Shaker family Kv channels are resistant to a Shaker-like 2 toxin (Shkl2) present in their own venom. We are expressing the Nematostella Shaker channels in Xenopus oocytes to expose them to Shkl2 to assess functional block using two electrode voltage clamp. The results obtained provide insight into the co-evolution of toxins and target channels in venomous cnidarians.

EFFECTS OF TYPE II DIABETES MELLITUS ON BIODISTRIBUTION OF ANTIFUNGAL DRUGS

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Background: The incidence of type 2 diabetes mellitus (T2DM) is increasing worldwide. T2DM impacts immunity, making diabetic individuals more susceptible to fungal infections. Currently, little is known about the effects of T2DM on antifungal treatment. The present study investigated how T2DM affects biodistribution of the antifungal drug Mycamine®. Methods: Mice (n=40) were maintained on a high fat diet for 4 weeks and induced to become diabetic with nicotinamide (60 mg/kg) and streptozotocin (100 mg/kg). Mice (n=40) maintained on a normal fat diet were used as a control. Both non-diabetic and diabetic mice received one dose of Mycamine (5 mg/kg). Blood and tissues were collected at 0.5, 1.0, 2.0, 6.0, 12, 24, 48, and 72h following the treatment (n=5 mice/timepoint). Drug concentration was determined via bioassay. Results: Drug serum concentration peaked at 0.5h in both groups. At 12 and 48h, the concentration was lower in serum of diabetic vs non-diabetic mice (p=0.0079). No drug was detected in serum at 72h in either group. At 0.5h, lung and spleen concentrations were lower in diabetic vs non-diabetic mice (p<0.02), with lung drug concentration peaking at 2h for diabetic vs 0.5h for non-diabetic mice. Conclusion: Mycamine cleared faster from the serum, lung and spleen of diabetic vs non-diabetic mice at early timepoints (between 0.5-2.0h). These results suggest that T2DM affects biodistribution of Mycamine by increasing the rate of clearance from the serum, and distribution and amount of the drug delivered to the organs.
Alzheimer’s Disease (AD) is a well known neurodegenerative disease associated with abnormal protein aggregation. Two of these proteins are tau protein and beta-amyloid protein, both of which have been shown to both work independently and simultaneously in the development of AD. The purpose of this study is to determine how beta-amyloid protein affects spatial learning and memory in a Drosophila melanogaster model. The Gal4-UAS system was used to express beta-amyloid protein in selective tissues of the brain, including the ellipsoid body which is homologous to basal ganglia, the mushroom bodies which are homologous to the hippocampus, and the entire brain. To study behavior, a visual thermal maze assay was used. The assay involved training flies to learn the location of a “cool spot” on a hot floor in relationship to surrounding visual cues. Each group of flies underwent five training trials. Then, the flies were tested in the absence of the cool spot. The time flies spent in the location of the cool spot as predicted by visual cues was examined. Results show that beta-amyloid expression in the ellipsoid body correlates with a slower recognition time of the cool spot. This suggests that beta-amyloid protein causes greater spatial memory degeneration when affecting a region homologous to the basal ganglia and may reflect issues with visual motor planning. These results are similar to results in comparable studies testing the effects of differential levels of tau protein expression on spatial memory; however, flies expressing altered levels of beta-amyloid are comparatively more fragile.

Organisms have limited resources to allocate to competing needs such as growth, reproduction, and defense against enemies. The growth-defense trade-off hypothesis suggests that faster flowering plants allocate less to defense against herbivores and pathogens compared to slower-flowering plants. Wild radish (Raphanus raphanistrum) is native only to the Mediterranean but is a serious weed in agricultural fields across the globe. Prior research has shown that weedy radish flowers faster than native radish, and this rapid flowering may be caused by higher levels of gibberellic acid (GA), a plant growth hormone. The application of GA to native radish resulted in the natives flowering faster but not as fast as weedy radish; however, GA did not affect weedy radish. These results combined with the trade-off hypothesis suggests that native radish receiving the GA treatment should be more susceptible to herbivores due to their faster flowering. We are measuring leaf area removed by herbivory for both the native and weedy radish, with and without the addition of exogenous GA. We predict that native plants treated with GA treatment will suffer more herbivory and flower faster than native controls. We expect GA to have no effect on the weedy radish, with both treatments receiving the highest herbivory due to their rapid flowering. A better understanding of weed allocation for growth and defense in native and weedy radish could improve weed control in agricultural fields.
The Impact of Adenylate Kinase Isoenzyme 4, a Mitochondrial Enzyme, on AMPK and Signaling Pathways

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Adenylate Kinases are phosphotransferase enzymes that catalyze the conversion of adenosine nucleotides. Adenylate Kinase 4 (AK4) is unique in its role in cellular bioenergetics, homeostasis and modulation of Adenosine 5’monophosphate activated protein kinase (AMPK) pathways. While it is known that AK4 expression levels impact adenosine nucleotide pool composition and activation of the AMPK pathway, little is known about whether these events are related or the mechanisms by which this occurs. This study explored the mechanism by which AK4 regulates AMPK signaling and whether AK4 expression dependent rises in Adenosine 5’monophosphate (AMP) activated the AMPK pathway. We hypothesized that reduced AK4 expression alters adenosine nucleotide pools to increase AMP levels, thereby activating AMPK signaling. Altered expression of AK4 was performed via siRNA in HK2 and HeLa cells with altered metabolic conditions. Activation of AMPK and other signaling pathways was validated using Western blot analysis. We show that loss of AK4 expression robustly activates AMPK signaling and induces AMPK-dependent cell biological effects such as enhancing autophagy. Expression of proteins signaling mTOR activation were not affected by AK4 siRNA knockdowns in HK2 cells. Consistent with our hypothesis, we also demonstrated that loss of AK4 increases cellular AMP levels in HeLa cells. We have identified a new link between mitochondrial biology and cytosolic AMPK signaling mediated through mitochondrial AK4 expression levels which may be dependent on the maintenance of adenosine nucleotide pools by mitochondrial AK4. We are currently assessing whether enhanced AK4 expression-dependent AMP levels are required for AMPK activation.

Rapid Development of Resistance to the Antiseptic Triclosan in Uropathogenic E. coli

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Antiseptics and antimicrobials are used widely in common household products, imposing a strong selection pressure on bacteria that may have connections with the current rapid and widespread rise in antibiotic resistance. This project explores the effect of long-term exposure to the common antimicrobial agent Triclosan on the uropathogenic E. coli strain CFT073. Triclosan, banned from consumer products in December of 2018, was used as an antimicrobial in a vast array of consumer products including toothpaste, soap, toys, detergents, and in the cleaning of surgical equipment. We used a disk diffusion assay to expose E. coli CFT073 and its isogenic ΔtolC mutant lacking the main efflux pump to Triclosan. Both the wild type and the ΔtolC mutant became resistant to high levels of Triclosan within just six days, as evidenced by shrinking inhibition haloes. We are also investigating whether the mutations that generated the changes in resistance to Triclosan are affecting phenotypes such as efflux and susceptibility to common antibiotics. Our results so far underscore the rapid evolution of resistance to antibacterial compounds and imply that E. coli can use mechanisms other than efflux via the AcrAB-ToIC efflux pump for preventing Triclosan from inhibiting cellular growth.
Revealing a Novel Interaction between Editing Factor RIP9 and an RNA of unknown function

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C-to-U RNA editing is a post-transcriptional modification that occurs in chloroplasts and mitochondria of most land plants, and it is essential for photosynthetic organelle function. Currently, 27 distinct editing sites have been published in chloroplast transcripts of Zea mays. RNA editing complex sufficient for activity in vascular plants requires several members of different protein families: PPRs, RIPS, ORRMs, OZs, and DEAH-box helicases. Assays attempting to construct active plant editosomes in vitro failed to demonstrate robust editing. Using size exclusion chromatography (SEC), we determined that RNA editosomes were large, stable and co-chromatographed with native RNAs. SEC fractions showing editing activity were larger than current models, and we hypothesize that still unknown factors might contribute to the mass and conformation of native editosomes. Editing complexes were shown to disassemble after an RNase A treatment. We have demonstrated that RNA editing activity for rpoC2 and rps14 transcripts survives immunoprecipitation using an antibody for editing factor RIP9. We have discovered that RIP9 complexes showed enrichment for an opening reading frame (ORF-X) RNA with unknown function. Also, our RIP-Seq has identified two putative editing sites with high percentage levels of conversion. Subsequent RNA extraction from anti-OZ1, anti-OTP86, and ORRM1 complexes followed by next generation and MinION sequencing will help to determine other RNA components of native editing complexes. RNA pulling assays will assist the assessment for the interactions of ORF-X and other RNAs with the PPR and non-PPR editing factors.

Electrochemistry (Teensy Stat)

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Electrochemistry is a concept learned by undergraduate students in their general chemistry course. Redox reactions are the most common way a student will learn electrochemistry. Later in their college career, electrochemistry is forgotten and sometimes never showed again. The Belmont’s Research Group has developed a low-cost device that will demonstrate electrochemistry to students in their upper-division courses. This device, fondly called the Teensy Stat is a potentiostat; that runs a Cyclic Voltammetry (CV) experiment. The CV outputs allows the researcher to monitor the current generated by the redox reaction, relative to the voltage stimulating the reaction. The resulting cyclic voltammograms, are shown as oxidation and reduction graph or either an oxidation graph or reduction graph, depending on the solvent or antioxidant used. The first swoop of the CV will be oxidation because the analyte is donating an electron to the electrode. The second swoop of the CV will be reduction because the analyte is accepting an electron from the electrode. This device will give a better understanding of electrochemistry to the students before they have graduated from an undergrad institution.
Using mutagenesis and omics methods to elucidate the regulation and metabolism of alkenones in E. huxleyi

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Emiliania huxleyi (E. hux) is one of the most abundant phytoplankton on this planet. In addition to producing intricate calcium carbonate cell coverings, they are one in five species on the planet to synthesize abnormally long chain fatty acids known as alkenones. Unlike other fatty acids carbon chain lengths range from 36-41. They have one to five trans double bonds and exist predominately as free fatty acids opposed to being esterified to a glycerol molecule. Most phytoplankton store energy in the form of triglycerides but on the other hand E. hux stores energy as alkenones. For many years' biogeochemists have used the alkenone desaturation index to estimate sea surface temperatures and construct paleoenvironments. The pathways involved in the biosynthesis and degradation of alkenones however, remain unknown. To determine whether elongases are involved in the synthesis of alkenones we used the K(3) herbicide Cafenstrole known to inhibit cell division and synthesis of very-long-chain fatty acids. To this end E. hux cells were plated on a lethal dose of Cafenstrole. Two spontaneous mutants were selected, and after growing in batch culture mutants were characterized. The growth rates were determined, and neutral lipids were extracted and profiled using gas chromatography-mass spectrometry (GC-MS). Genomic DNA and RNA were subsequently extracted and sent for sequencing.

Gold Nanoparticle Synthesis for Conjugation to NVC Nanodiamonds for Fluorescence Enhancement for Biodetection Methods

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Imaging Nitrogen Vacancy Center (NVC) SiO2 functionalized nanodiamonds (NDs) is useful for their potential applications in biolabeling and biosensing due to their electron spin properties, biocompatibility, molecular components, and stability. However, imaging requires high level of light, which increases background noise from tissues. Conjugating Gold Nanoparticles (AuNPs) to the surface of SiO2-coated NDs, allows imaging detection at a much lower level of light, thus preventing background fluorescence from surrounding biologically active materials. NVC nanodiamonds and AuNPs Gold plasmons are metallic nanoparticles which greatly increase the luminescent properties of NVC nanodiamond. The primary goal was to conjugate SiO2 functionalized NVC nanodiamond surfaces with AuNPs in order to augment the nanodiamonds for superior detection while utilizing light microscope at lower frequencies. Viability of SiO2-coated NDs was increased when conjugated with AuNPs. Furthermore, downstream application of the NDs is not affected by addition of AuNPs. Conjugating the two nanoparticles required vigorous stirring along with the addition of base, water, and linker molecules. Both AuNPs and SiO2 coated nanodiamonds were imaged via Scanning Electron Microscopy (SEM) and identified via Dynamic Light Scattering (DLS). Results were studied in detail with applications such as Igor and ImageJ in order to configure intensity, volume, and growth counts from instrumental data. Upon achieving successful results, the conjugated particles could be exploited for biodetection and biolabeling applications in the near future.
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Cal Poly Pomona

This study tested the efficacy of a liposomal Aspergillus vaccine (VesiVax LAsV), in protecting against A. fumigatus challenge (ATCC#13073) with or without concomitant antifungal drug treatment. The vaccine contained Aspergillus proteins Aspf3 and Aspf9, and the adjuvant lipidated tuaresol. Six-week old Swiss Webster mice were vaccinated with LAsV (Molecular Express, Inc.) subcutaneously on d0, with intranasal boosts on d21 and d42. Control mice received phosphate buffered saline (PBS). Before challenge, spleens and blood were collected (n=5/group) for ELISpot and agglutination immunoassays and remaining mice were immunosuppressed with triamcinolone. On d56, mice were intranasally challenged with A. fumigatus (1.5*10^7 spores/mouse). Some groups were given a short course of 7.5 mg/kg liposomal amphotericin B (AmBisome, AmBi, Gilead Sciences Inc.) intravenously post-challenge. Lungs were collected (n=7/group) 7 days post challenge for fungal burden, and remaining mice (n=9/group) were monitored for survival to d77. LAsV vaccinated mice yielded reduced lung fungal burdens compared to control mice (p=0.0379), and had 55% survival versus 22% for mice given AmBi alone or PBS. ELISpot cytokine analysis showed that LAsV vaccinated mice had more IL-4 than IFN-γ secreting splenocytes following incubation with Aspf3 and Aspf9 (p=0.0178). Agglutination titers demonstrated that LAsV vaccinated mice had increased anti-A. fumigatus spore antibodies in the serum than control mice (p=0.0009). LAsV vaccination before Aspergillus challenge, with or without AmBi treatment, provided more protection than AmBi alone. Elevated antibody titers correlated with protection, and increased IL-4 secretion indicates a Th2 response. The LAsV has the potential to be used prophylactically to protect patients from pulmonary aspergillosis.

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Emiliania huxleyi is one of the most abundant phytoplanktons found in the euphotic zone of the ocean (Kondrik et al., 2019). As a coccolithophore, E. huxleyi produces intricate calcium carbonate disks known as coccoliths that form a coccosphere which surround the cell (Chairopoulou et al., 2018). Upon collection in 1991 off the coast of Peru, E. huxleyi cells were isolated and sent to two culture collection laboratories. One at the National Center for Marine Algae at the Bigelow laboratory in Maine and the other at the Plymouth Marine Algal Collection in England. After roughly 20 years in culture the strain, CCMP 1516, lost its ability to calcify while the strain, PLY 217, retained its ability to calcify. Both strains were analyzed and were found to be isogenic, meaning that they have closely similar genotypes. The question set out to answer was, whether epigenetic changes may be responsible for the phenotypic differences in these isogenic strains. Bisulfite sequencing and gene expression analysis through RNAseq was carried out to independently validate methylation levels on a list of candidate genes known to be susceptible to epigenetic modifications between 1516 and 217. Real time RT-PCR is being used to validate gene expression differences of differentially methylated genes. Preliminary results show some genes such as the one responsible for the Ca2+/Mg2+-permeable cation channels transient receptor potential protein to be differentially expressed in 217 and 1516. Future directions include looking at genome accessibility and histone modifications.
EMMANUEL SOLIS, Carlos Luna Lopez
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Food, plant and synthetic based wax (microcrystalline, candelilla, carnauba, petroleum) are widely used in cosmetics and personal care products. However, due to climate change and increase in soil pollution there is a reduction in the production of these waxes. Therefore, identifying alternative wax for using in the cosmetics and personal care products will have significant impact in products cost and for consumer affordability. A recent study has suggested that alkenones, a large chained unsaturated methyl and ethyl n-ketones could be substituted for food and plant-based wax. Alkenones are produced by marine algae which can be cultured and are abundant in ocean. To further determine if alkenones produced by marine algae show characteristics of a wax, Alkenones were isolated from marine coccolithophorid Emiliania huxleyi in a chloroform solution. A monolayer of alkenones at the air-water interface was formed in a Langmuir Trough. We used the Thin Film Deposition Method to create a layer-by-layer thin film of alkenones in a glass substrate. We analyzed the hydrophobicity by measuring the contact angle of water droplets. We also analyzed the UV absorption of alkenone thin films using a spectrophotometer. We found that thin films of alkenones are capable of absorbing UV light, a characteristic that could make alkenone films more special compared to traditional waxes. Thin films of alkenones also showed a certain level of hydrophobicity with a contact angle of 70 degrees. These results seem to indicate that alkenone films could become a sustainable wax alternative.

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CSU Long Beach, McNair Scholars, Bridges to the Baccalaureate

The amygdala is a brain region responsible for coordinating autonomic, behavioral, and endocrine responses to environmental stimuli with emotional content, of which are different between the sexes. Accompanying functional differences, neural structures of the amygdala are found to be sexually dimorphic. These differences are dependent on androgens and androgen receptor (AR), but the underlying molecular mechanisms are unknown. This study was to identify proteins differentially expressed in the developing amygdala of male and female mice using proteomics approach. Male mice carrying the testicular feminization mutation (Tfm) were included to investigate if the differences in protein expression were regulated by AR during early development. Tfm mice display a female phenotype in reproductive structure and behavior. Protein samples extracted from the amygdala of Tfm mice and their wild-type littermates (21 days of age, N=9 per group) were separated by two-dimensional (2D) gel electrophoresis. The resulting protein spots were visualized, and their intensities measured. Using Progenesis, a total of 300 protein spots on the 2D gels showed significant differences among the three groups, and 31 of them displayed a fold-change of 1.5 or greater. Three spots were excised from gels, followed by in-gel digestion and protein identification using matrix assisted laser desorption ionization-time of flight mass spectrometry. Mass spectrometry analysis identified nucleoside diphosphate kinase (NME1) from one of the three spots. We will use immunoblotting to verify and profile the sex difference in NME1 expression in the mouse amygdala and further investigate the physiological role of NME1 in brain sexual differentiation.
Multi-Isotopic Fractionation of Water From Sublimation at Low Temperatures

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Understanding how astrophysical processes like diffusion, evaporation, and condensation of volatile ices affects the ratios of isotopes can help us better understand observations of isotopic variation in astrophysical systems. For example, the sublimation of water-ice from astrophysical and planetary surfaces such as interstellar dust, comets and asteroids at low temperatures is expected theoretically to result in significant shifts in the isotopic composition of the residual water ice. Using a UHV system with closed-cycle He cryostat and a cavity ring-down isotope spectrometer (CRD), we developed a protocol for measuring changes in the ratios of D/H, 18O/16O, and 17O/16O that result from the sublimation of water ice at 155 K. In this presentation, we discuss the challenges and lessons learned to achieving experimental conditions that mimic astrophysical environments. Results from our experiments, including instantaneous fractionation factors associated with hydrogen and oxygen isotopes will be presented. To assess whether the experimental conditions present in the UHV chamber are adequate for simulating sublimation into the near perfect vacuum of space, we developed a detailed model of the isotopic fluxes associated with the water-ice surface, vacuum chamber walls, and pumping provided by a magnetically levitated turbo pump. This model incorporates a transition-state-theory (TST) based representation of surface potential energies and associated isotopic fractionation factors. Using this model, we estimated the magnitude of water recondensation onto the cold-surface and calculated the associated effects on the isotopic composition of the residual water ice compared to the theoretical values expected for pure sublimation.

Expansion of Scope for Nickel-Catalyzed Cross-Electrophile Couplings of Sulfonamides for Cyclopropane Synthesis

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The cyclopropane motif is important in medicinal chemistry because the C–H bonds have increased metabolic stability in drug molecules, therefore developing methods to form the moiety is important. This work attempted to form cyclopropane through a transition metal-catalyzed cross-electrophile (XEC) reaction. XEC reactions, an alternative to cross-coupling (XC) reactions, are important because they allow for facile construction of C–C bonds without the use of organometallic coupling partners. Previous studies indicate that XECs of amines typically require strained or charged starting materials, but this method utilized unstrained and uncharged alkyl amines. This work successfully expanded the scope of sulfonamide XEC reactions for cyclopropane synthesis to include two heterocycles, a carbazole and a methylated indole. Key steps for the substrate synthesis include Grignard additions and Hydroboration oxidations. Additionally, the synthesis of an enantioenriched piperidine substrate was carried out in order to determine the stereochemical outcome of the XEC. All intermediates were purified via flash column chromatography and structures were confirmed by proton NMR. Melting points and high-resolution mass spectrometry were used to characterize substrates.
Designing probes for the real time tracking of heterochromatic epigenetic marks

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The presence of epigenetic marks on histones has been well documented and is a vital part of gene regulation in cells. One of the most common epigenetic marks is methylation of lysine and arginine on histone tails. One such example is methylation at K9 on H3 (H3K9), the dominant mark signaling gene repression. The addition of these methyl groups direct local assembly of structural proteins that tightly package the chromatin eventually inhibiting gene expression co- or post transcriptionally. We know these marks are important, however, a method of easily detecting and visualizing them does not exist. Methyl groups are difficult to observe experimentally and currently the only way to isolate methylated nucleosomes is via immunoprecipitation. This procedure yields all the methylated DNA in the entire cell and has no specificity for sequence. My lab developed a methodology which will allow us to visualize methylation of chromatin in real-time using fluorescently labeled proteins that can specifically recognize the epigenetic mark. Many proteins exist in nature that can bind preferentially to the marked lysine over the unmarked lysine. We expressed and purified 9 specific methyl lysine reader domains and through florescence polarization we measured their affinity to the H3K9 trimethyl mark on a small peptide. Moving forward, we will characterize how these peptides impact full nucleosome function and reader protein binding kinetics. By creating a system to visually track epigenetic modifications we can more accurately study epigenetic phenomenon and learn more about control mechanisms which underly genetic regulation and cellular life cycles.

Solid-Phase Synthesis of Modified Peptides Based on PGC-1 alpha, a Regulator of Cellular Metabolism

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Recent studies show an interplay between arginine methylation and serine phosphorylation within the Akt binding motif in proteins. Peroxisome proliferator-activated receptor-gamma coactivator 1alpha (PGC-1alpha) is a key regulator of energy metabolism induced during fasting and elevated in diabetes. We anticipate a similar interplay in PGC-1alpha which also contains several Akt binding motifs (RXRXXS/T). We set out to study this interplay by using solid-phase peptide synthesis (SPPS) to first make modified peptides based on PGC-1alpha containing the Akt binding motif. SPPS will allow for the synthesis of peptides with sequences either lacking the residues modified, or containing modified residues (methyl or phosphate groups) and thus help elucidate the effects of methylated arginine residues on neighboring serine phosphorylation within the Akt motif. SPPS is an established and robust procedure, however preliminary work shows that these peptide sequences require further optimization due to the nature of the size and/or charge of amino acids such as arginine. We plan to mitigate synthesizing sterically encumbered peptides by double coupling arginine, optimizing coupling reagents and/or extending the coupling time. The peptides will then be used as substrates for enzymatic methylation and phosphorylation reactions, respectively. Because PGC-1alpha directly modulates the production of glucose and has been shown to promote the use of fatty acids stored in adipose tissues as a source of energy, it is implicated in a variety of vital metabolic processes. Revealing the regulatory function of PGC-1alpha may contribute to improving targets for pharmacological treatment in type 2 diabetes and obesity.
The enteric nervous system (ENS) mostly arises from vagally specified neural crest cells that migrate along the gastrointestinal tract, proliferate and differentiate into enteric neural crest cells (ENCC). Failure of ENCC migration leads to anomalies in the ENS resulting in ineffective intestinal motility conditions such as Hirschsprung Disease. Glial cell-derived neurotrophic factor (GDNF) is implicated in enhancing migration, proliferation, and differentiation of embryoid body derived ENCC after two-week exposure. We hypothesized that GDNF treatment promotes differentiation and migration in a human induced pluripotent stem cell (iPSC)-derived ENCC model. Human iPSC were directed toward ENCC in a 15-day suspension culture. The experimental group received 25 ng/mL of GDNF on day 11 and day 13, while the control group received no additional GDNF. On day 15, differentiated ENCC formed neurospheres and were collected for qPCR and immunofluorescence (IF) staining analyses. Single-celled ENCC neurospheres were seeded onto monolayer culture to perform an in vitro scratch assay. After wounds were created, images were taken every 24 hours for three consecutive days to measure migration across the defect. Migration rates were calculated by ImageJ. After four days of GDNF treatment, there were no significant differences on day 15 between the experimental and control group of gene expression, IF staining or migration rate. Therefore, the addition of GDNF for a short period showed no improvement compared with the control group. For future experiments, we would lengthen both differentiation and GDNF exposure duration to test the potential GDNF effects in iPSC model.
Resorcin[4]arene cavitands represent a versatile framework from which to build molecular capsules capable of host-guest interactions. In this work we hope to contribute to the growing body of resorcin[4]arene capsules and investigate their ability to conformationally open and close in response to variable conditions such as temperature, pH, solvent, and guest interactions. We propose the synthesis of four rigid, covalently assembled molecular capsules as modified designs of a previously published flexible, hinged, molecular capsule from our lab. These new capsules are designed to maintain a more rigid framework by way of two linkers between each resorcin[4]arene cavitand rather than one, and with variable, conformationally switchable, functional groups to dictate guest encapsulation. We report the synthesis and characterization of major starting materials toward the production of these capsules, as well as the findings of two ongoing trials attempted for synthesis of our target capsule products.