BUILDing SCHOLARS
THE UNIVERSITY OF TEXAS AT EL PASO

DIVERSITY PROGRAM CONSORTIUM
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3rd Annual BUILDing SCHOLARS Symposium and Consortium Meeting

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Texas The University of Texas at Austin
UTHealth The University of Texas Health Science Center at Houston

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Session 1

Addiction 1

The Social Norms and Risk Perceptions of Alternative Cigarette Usage in College Aged Students

Raymond Oliva[1^], Gabriel Frietze[2*], Jessica M Shenberger-Trujillo[2*]

[1] Department of Psychology, The University of Texas at El Paso.
[2] School of Pharmacy, The University of Texas at El Paso.

Research suggests that mortality rates for smokers are approximately three times higher than for non-smokers. Many laws and regulations have been imposed with aims of reducing tobacco use, however, the tobacco industry has adapted to these regulations by introducing Novel Tobacco Products (NTP) such as snus, dissolvables, and e-cigarettes. These products are often marketed as safer alternatives to traditional cigarettes and useful for quitting smoking. An aim of this study was to examine the extent to which young adults' (N=87; Mage=22.9, SD=4.90) have used various products (i.e., e-cigarettes, nicotine gum) and services (i.e., calling a helpline, counseling) to attempt to quit smoking cigarettes. Preliminary results suggest that nicotine gum was the most reported method that participants would use to quit using tobacco (M=2.46, SD=1.44). In contrast, Zyban® (M=1.72, SD=1.03) was the least reported method that participants would use to quit using tobacco. Furthermore, a significant difference in the likelihood to use a product to quit smoking (M=2.04, SD=0.95) versus a service (M=2.38, SD=1.26; t(42)=-2.06, p=.046; Cohen's d=0.30) was detected in participants who reported that they have used a tobacco product in their lifetime (n=43). Exploratory analyses suggest education (p=.247) and annual household income (p=.433) are not associated with the use of tobacco products or services to quit smoking. Findings from the current study suggest that participants are more likely to seek out a service to quit smoking than using tobacco products to quit smoking. These findings have implications for designing public health interventions aimed at reducing smoking in young adults.

Funding Source: NIH-NIGMS, Paso Del Notre Health Foundation

Correlating Human Plasma Biomarkers To Susceptibility to Alcoholism

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[2] Department of Biological Sciences, Southwestern Indian Polytechnic Institute.
[3] Department of Biological Sciences, UT Southwestern.
[4] Department of Psychology, The University of Texas at El Paso.

Alcoholism is a worldwide issue affecting millions of people every year often arising from simple social drinking. It is currently unclear why certain individuals have a predisposition for developing alcohol abuse while others do not. Identification of a panel of biomarkers that could differentiate an individual's susceptibility to becoming alcoholic would therefore be highly desirable. In this study, blood samples from recovering alcoholics were used to correlate susceptibility to alcoholism to changes in the allostatic load of certain biomarkers. Blinded and de-identified patient blood samples were provided by Dr. Bryon Adolf from UT Southwestern University. Milliplex and 3-Cat ELISAs were used to analyze biomarkers in the blood plasma. Alcoholic patients had significantly higher blood plasma levels of melatonin compared with control samples, despite sample collection at the same time of day. This could suggest that alcoholics experience increased tendencies toward tiredness. In addition, alcoholics tended towards increased serum plasma levels of cortisol and oxytocin, biomarkers of increased stress. Furthermore, alcoholics had increased serum plasm levels of TNF-α indicative of enhanced inflammation potentially caused by tissue damage in the liver, though at the time of sampling, patients were not experiencing liver disease. This study could open the door to identify selected biomarkers to determine the susceptibility to alcoholism.

Funding Source: NIH-NIGMS

Cancer
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T-cell Acute Lymphoblastic Leukemia Cells Dependency on C-C Chemokine Receptor 7 for Central Nervous System Infiltration

Jailene D Amparan^, Anahi Sanchez^, Miguel A Carrillo-Alvarad^, Charles Bill^, Colin A Bill*, Charlotte M Vines*

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T-cell acute lymphoblastic leukemia (T-ALL) is a blood cancer most commonly found in children and adolescents that can invade the central nervous system (CNS). Inside the CNS, T-ALL becomes inaccessible to chemotherapies that circulate in the blood, necessitating the direct application of harmful drugs and ionizing radiation to the CNS. CCR7 binds to it ligand C-C motif chemokine ligand 19 (CCL19), which promotes T-ALL invasion of the CNS. Therefore, we hypothesize that if we can block CCR7, we can block T-ALL invasion of the CNS, and perhaps prevent recirculation into the CNS once the cells exit to the periphery. To study this we compare CEM cells that express endogenous CCR7 and migrate into the CNS to DND41 cells, which do not express CCR7 endogenously and also do not invade the CNS. We hypothesize that expression of luciferase in the T-ALL cells will allow us to follow the cells during progression of T-ALL in the presence or absence of CCR7 blocking peptides. Using a Luciferase-2 expressing lentivirus we are transducing CEM, DND4, and another CCR7 expressing cell line, Hut78 to use in an in vivo model of T-ALL. These cells will allow us to track the localization of T-ALL CEM, DND41 and HuT78 cells by bioluminescent imaging in a live animal to determine if CNS infiltration persists in the presence of CCR7 antagonists. Ultimately, these studies will allow us to develop platforms for pharmaceuticals to prevent T-ALL from invading the CNS.

Funding Source: NIH-NIGMS

The role of Prostate Specific Membrane Antigen (PSMA) on One Carbon Metabolism of Prostate Cancer

Luisa F Castillo^

Department of Chemistry and Biochemistry, The University of Texas at El Paso.

Prostate cancer (PC) is the most commonly diagnosed cancer in the US. Cancer cells survive in the nutrient-poor, hypoxic environment created by rapidly growing tumors by altering their metabolism. These metabolic alterations are fundamental to their growth in situ as well as their progression to metastasis which underlies the majority of disease-related mortality. The transmembrane peptidase Prostate Specific Membrane Antigen (PSMA) is progressively upregulated in ~80% of tumors during PC progression and correlates negatively with prognosis. Additionally, in advanced PC, PSMA cleaves poly-g-glutamated-folates leaked into the tumor microenvironment by apoptotic/inflammatory epithelial cells producing free glutamate and folic acid. Previously, we reported that the expression of PSMA promotes increased tumor cell survival in hypoxic environments. To investigate how these hypoxia-induced PSMA-dependent survival mechanisms affected folate driven one-carbon metabolism, we used a CRISPR/Cas9 engineered panel of PSMA-positive ($PSMA^{scr}$) and PSMA-null ($PSMA^{KO}$) human PC cell lines (LnCaP, 22rv1). Western blot and RT-qPCR analysis of $PSMA^{KO}$ cells incubated under hypoxic conditions (1% oxygen) for 0-3hr revealed a switch in the requirement of one-carbon units for nucleotide synthesis, methylation, and reductive metabolism. Additionally, there was a measurable difference in the glucose-dependent aerobic glycolysis typical of cancer cells to anaerobic oxidative phosphorylation characteristic of controlled proliferation and decreased resistance seen in less aggressive tumors. These results suggest that PSMA expression on tumor cells confers resistance to hypoxia and contributes to tumor progression via adaptive changes in the one-carbon pathway, thus supporting complete disruption of PSMA as a promising therapeutic option in management and treatment of PC.

Funding Source: National Cancer Institute, NIH-NIGMS

Improving the efficacy of dendritic cell tumor vaccines

Montserrat C Garcia Arreguin[1^], Vanaja Konduri[2^], Matthew Halpert[2^], Jonathan Vazquez-Perez[2^], Irene Chen[2^], Briana A Burns[2^], Damilola G Oyewole-Said[2^], William K Decker[2^], Jonathan M Levitt[2]*

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[2] Department of Pathology and Immunology, Baylor College of Medicine.

Our research group focuses on antigen-presenting dendritic cells (DCs) as a vaccine platform to treat cancer. Although DC vaccines have been synthesized with encouraging results, the conditions in which the antigens are introduced into the DCs is a source of optimization to enhance vaccine efficacy. We have previously shown that the inhibitory receptor, CTLA-4, is downregulated in double-loaded DCs which strongly activate T cell responses. This allows us to utilize intracellular CTLA-4 as a readout for effective antigen loading of DCs. The purpose of this project is to evaluate one factor in the antigen loading process of DC vaccines, serum concentration, for the ability to induce activation of DCs and thereby enhance anti-tumor responses. Bone marrow-derived DCs were produced from mice by culturing in cytokines for 6 days. The DCs were loaded with peptide and protein in varying concentrations of complete or heat-inactivated mouse serum for three hours. After incubation, the cells were matured using a maturation cocktail for 48 hours. Expression of DC-specific maturation markers and CTLA-4 were measured. We found that CTLA-4 expression decreased with decreasing mouse serum concentrations. Additionally, the trend remained unchanged when serum growth factors were denatured. These data suggest that serum proteins are likely to be competing with antigen loading of DCs. Further studies will be done to demonstrate that DCs loaded in low serum concentration are more effective at activating T cells and to determine the mechanism by which double loading enhances DCs ability to activate T cells.

Funding Source: NIH-NIGMS, NCI, NIH-NIAID

Recommended Citation:
Garcia Arreguin, Montserrat; Konduri, Vanaja; Halpert, Matthew ; Vazquez-Perez, Jonathan; Chen, Irene; Burns, Briana; Oyewole-Said, Damilola; Decker, William; Levitt, Jonathan. "Improving the efficacy of dendritic cell tumor vaccines" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1633

Closing the Gap: Interpreting Upstream Determinants Impacting Breast Cancer Treatment Decisions for Hispanic Women

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[2] Department of Health Solutions, arizona State University .

Despite similar rates in breast cancer screening between Hispanic and White women, Hispanic women in Arizona are diagnosed at more advanced stages, are offered fewer treatment options, and suffer from disproportionately higher mortality rates. Hispanic women simultaneously experience a parallel continuum of social determinants of health that exacerbate factors contributing to disparities in breast cancer outcomes, including low socioeconomic status, language barriers, racial and ethnic discrimination, lower health literacy, lack of trust, and fears regarding immigration status. A qualitative snapshot study was conducted to understand the perspectives of Hispanic breast cancer patients, how upstream factors impact their treatment decisions, and how those perspectives compare with the perceptions of their providers. In an attempt to decrease mortality rates and facilitate better care, a mixed methods open-ended interview was conducted to examine the patients' stories, attitudes, and beliefs. Analysis between patient and provider surveys are still ongoing, however, findings indicate key themes for both patient and provider perceptions to barriers in care and treatment, as well as discrepancies between both groups. This study underscores the gaps that exist in provider perceptions and patient experiences that extend beyond the clinical walls. Interpreting these perspectives will have significant implications in reducing disparities, improving equity, and recommend local and state policy for vulnerable communities.

Funding Source: NIH-NIGMS

Rgs8 and Rgs16 are Tumor Suppressors in Pancreatic Ductal Adenocarcinoma

Brianna B Sanchez[1^], Shreoshi Pal Choudhuri[2^], Thomas M Wilkie[2]*

[1] Department of Biological Sciences, The University of Texas at El Paso.
[2] Pharmacology, UT Southwestern.

Kras oncogenic mutations (e.g. KrasG12D) occur in 95% of human Pancreatic Ductal Adenocarcinomas (PDA); the deadliest of all major-cancers with a median survival of 6 to 12 months after diagnosis. Pharmaceutical treatments are desperately needed but characterization of the disease and a proper PDA model must first be accomplished. The KCR8-16 mice we developed are an excellent mouse model for identification, characterization, and in-vivo validation of potential PDA therapeutics. Kras can be activated by protein kinase and G-Protein Coupled Receptor (GPCR) signaling. Activated alleles of Gq that are resistant to Regulator of G-protein Signaling (Rgs) inhibition are found in benign human PDA precursors. Previously, we reported Rgs8 and Rgs16 are in-vivo reporters of Kras activity in pancreatic intraepithelial neoplasia (PanIN), intraductal papillary mucinous neoplasm, and PDA progression in KrasG12D, P48Cre-Rgs16::GFP (KC) mice. To identify the role of Rgs8 and Rgs16 in PDA, we crossed Rgs8-16 double knockout into KC mutant mice (KCR8-16). We found that deletion of Rgs8 and Rgs16 in KC accelerated PDA progression. Additional pancreatic stress evoked by various Caerulein dosages caused aggressive, pancreas-wide PDA progression within seven days in KCR8-16 mice. We are characterizing our novel KCR8-16 mice via histology, immunofluorescence, and immunohistochemistry. Our data suggests KCR8-16 mice have a more aggressive form of PDA and worse survival than KC mice because Rgs16 protects against PDA initiation and progression. Furthermore, KCR8-16 mice can be used as an excellent model for identification and rapid in-vivo validation of PDA therapeutics.

Funding Source: NIH-NIGMS. NCI CA161624 and by NCI CA161624 and UT Southwestern Cancer Center Pilot Project Award to RAB and TMW.

Recommended Citation:
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Degenerative And Chronic Diseases 1

Investigating the Role of the Mevalonate Pathway in the Intestine

Claudia Ayala[1^], Alexandria Doerfler[2^], William Lagor[2*]

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Statins, the primary class of drugs prescribed to lower cardiovascular disease risk from hypercholesterolemia, work by inhibiting 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR), the rate-limiting enzyme in cholesterol biosynthesis (mevalonate pathway). However, the majority of statin research has centered on the liver, and there is a surprising lack of knowledge regarding the importance of the mevalonate pathway in the intestine. We hypothesize that HMGCR is required for proper lipid absorption in the intestine. To test this, we generated mice with an intestine-specific deletion of the Hmgcrgene. The intestine was isolated from these mice and sections of the duodenum, jejunum, and ileum were subjected to histology for hematoxylin and eosin (H&E), Ki67, and cleaved Caspase-3. Expression of Hmgcrand sterol related genes were measured by quantitative polymerase chain reaction (qPCR). Hmgcrwas successfully knocked out in the intestine based on mRNA measurements, and we also observed compensatory upregulation of several other enzymes in the mevalonate pathway. We found that Hmgcrintestinal knockout mice had significantly lower body weights from weaning through 5 weeks of age. Additionally, H&E staining showed significantly increased crypt height (~2-fold) and dysmorphic villi, suggesting a regenerative response. These data indicate that Hmgcr is required to maintain normal body weight and intestinal function. Further studies are needed to fully understand the mechanisms behind these alterations in body weight and intestinal morphology, and the role of the mevalonate pathway in absorption of dietary lipids.

Funding Source: NIH-NIGMS

Recommended Citation:
Ayala, Claudia; Doerfler, Alexandria; Lagor, William. "Investigating the Role of the Mevalonate Pathway in the Intestine" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1636

Theoretical and experimental study of the crystallographic structure of cardiac myosin in neonatal rats by polarization reserved second harmonic generation microscopy

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[2] Department of Bioengineering, Clemson University.

Cardiac hypertrophy, is a cardiac disease caused by genetic mutations and/or alterations in mechanical loads of cardiac myosin. Due to the protein's involvement, it is essential to understand the molecular structure changes of myosin during cardiac hypertrophy. The heart of a neonatal mammal also undergoes a significant cardiac hypertrophy process after birth. Second harmonic generation (SHG) microscopy has been widely applied for visualizing noncentrosymmetric biomolecules. In this study we used PR-SHG microscopy to image the structure development from neonatal rat hearts at day 1,3,5,7,10 and 20. Myocardium samples were isolated from newborn rats at each day. The hearts were embedded in optimal cutting temperature compound (OCT compound) at -20 °C, and 10-μm thick sections were sliced before imaging. As the days continued, the values of χ_{31}/χ_{15} remained approximately unchanged at 1.20, but the values of χ_{33}/χ_{15} were significantly reduced from 1.04 to 0.74. Since χ_{33}/χ_{15} describes the orientation angle of the myosin molecule, the decrease of χ_{33}/χ_{15} from day 1 to day 20 indicates that the orientation angle of the myosin molecules is more uniform. SHG can effectively retrieve the value of nonlinear susceptibility tensor and detect the changes in the structure and orientation of myosin molecules. According to the results of our study, the orientation angle of myosin, in the heart of a neonatal mammal, gradually became more consistent under the increasing mechanical contraction force. The results of this study can provide a meaningful reference for understanding the microscopic mechanism of cardiac hypertrophy.

Funding Source: NIH-NIGMS

Temporal Control of TDP-43 Protein Expression Using Gene Switch

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Amyotrophic Lateral Sclerosis (ALS) is a fatal progressive neurodegenerative disease that affects motor neurons. Although this disease is poorly understood, an aggregated protein, TAR DNA Binding Protein 43 (TDP-43), has been identified in familial and sporadic ALS patients. Various research models, such as mouse, zebrafish, Drosophila, and worms, have been used to better understand TDP-43 and its role in ALS. Drosophila is an inexpensive model and shares similar metabolic pathways with humans. In this project, we use Elav-GAL4 Gene Switch System. This system works by crossing driver lines that express Elav with UAS-reporter lines with inserts of a target gene. In the presence of a hormone, drug (RU486) food, Elav then attaches to the GAL4 binding sites and the target protein, TDP-43, is expressed. We created three genetic crosses: a white control group, human TDP-43 wild type, and disease causing variant of TDP-43. We placed these genetic crosses in standard fly food for 5 days, collected 1st and 2nd instar larvae, and transferred the larvae into varying concentrations of RU486 food for 2 days. After the two-day exposure in RU486 food, we collected larvae samples from each genetic cross for Western Blot Analysis. This analysis demonstrated that exposure to higher concentration of RU486 resulted in greater TDP-43 expression. In conclusion, this indicates that Elav-GAL4 Gene Switch System successfully induced TDP-43 protein and will serve as an in-vivo representation of TDP-43 progression through time.

Funding Source: NIH-NIGMS, NIH, MDA, HHMI Gilliam Fellowship, Undergraduate Biology Research Program (UBRP, University of Arizona)

Recommended Citation:
Esparza, Aibhlin; Shreiner, Dakotah; Manzo, Ernesto; Zarnescu, Daniela. "Temporal Control of TDP-43 Protein Expression Using Gene Switch" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1630

Simulated Sleep Apnea Induced Changes in Carotid Body Signaling

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Sleep apnea is a respiratory disorder that increases blood pressure in part by activating the sympathetic nervous system (SNS) releasing norepinephrine (NE). Our previous studies found that exposing rats to short periods of hypoxia during sleep to simulate sleep apnea (IH) inhibited production of the vasodilator, hydrogen sulfide (H_2S) in arteries by downregulating the enzyme cystathionine gamma lyase (CSE). Another group reported that IH increases production of H_2S within the carotid body (CB) by upregulating CSE. The CB reflexively increases SNS activity when oxygen is low, therein an increase CSE in the CB appears to increase SNS activity and blood pressure. Inhibiting CSE increases blood pressure in normal rats but decreases blood pressure in IH-exposed rats. We hypothesized that IH increases CSE expression in the CB to elevate SNS release of NE. Rats were exposed to either IH or SHAM conditions for 14 days and then euthanized. Urine and plasma were collected to measure NE levels to evaluate SNS activity while CB were collected to measure CSE protein expression using immunohistochemistry. Data suggests NE levels are not different in either plasma or urine between IH and SHAM groups. CSE staining appears qualitatively greater in the carotid bodies in rats in the IH group compared to rats in the SHAM group. Future directions will evaluate CSE expression in carotid bodies through qPCR.

Funding Source: NIH-NIGMS

Characterization of mechanical properties of porcine vein following thrombosis

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Every year, in the United States alone, from 300,000 to 600,000 people suffer venous thromboembolism, with only 72% of the people surviving past the 30-day mark. Among those, 30% have repeat presentation after 10 years.

Most studies exploring vessel mechanics have focused on arteries. However, arteries and veins have vast differences in their structure and function. Current literature lacks adequate information about venous mechanics. This study aims to understand the changes in the mechanical properties of veins following thrombosis, evaluating its changes through a determined timespan.

The pigs were first injected with thrombin at the infrarenal area of the Inferior Vena Cava (IVC). Then, the pigs were euthanized at 1-week intervals, from 1 to 5 weeks. Next, the IVC and the iliac veins were extracted; the suprahepatic region of the vein was obtained as a control due to its separation from the injection site. Veins from healthy control pigs were also obtained. The samples were then sectioned into longitudinal and circumferential strips, and the smallest cross sectional area of each strip was measured before the uniaxial tensile test to convert load- deformation raw data to stress-strain.

Significant differences were found between the elastic modulus of the healthy IVC and thrombosed IVC samples at weeks 1, 2, and 4 weeks. This data suggests that remodeling occurs to the venous wall in response to thrombosis and illuminates the needs for further studies to understand venous mechanics.

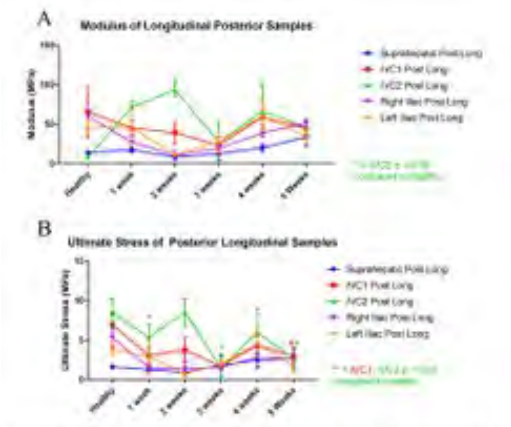

Figure 1: Elastic Modulus (A) and Ultimate stress (B) of Posterior longitudinal samples. Significant differences are seen in both stiffness and ultimate stress of the IVC2 samples, where the thrombus was injected and the thrombus formed, suggesting that the presence of thrombus induces remodeling in the venous wall.

Funding Source: NIH-NIGMS, NSF

Investigating the role of retinoic acid signaling in modulation of trabecular meshwork matrix

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Primary open angle glaucoma (POAG) is characterized by an increase in intraocular pressure within the eye, and dysregulation of the conventional outflow pathway through the trabecular meshwork (TM). It's been suggested that TGFβ signaling plays a role in the progression of POAG. Further, as well retinoic acid (RA) signaling has been reported to inhibit TGFβ signaling in human fetal palate mesenchymal cells. In this study, we investigated whether retinoic acid signaling had any role in regulation of extracellular matrix proteins of the TM, such as fibronectin and various collagens. Diseased primary TM cells were used alongside normal TM cells, and both were subjected to exposure of various RA agonists and an antagonist at differing concentrations. Quantitative PCR (qPCR) as well as high content imaging (HCI) were utilized to assess this question. HCI and analysis suggested that the agonist all-trans retinoic acid (ATRA) impeded fibronectin synthesis at higher concentrations (1uM – 10uM). By contrast, qPCR indicated that collagen synthesis persisted in both types of TM cells, and the agonist ATRA slowed the synthesis of fibronectin in diseased TM cells. In conclusion, the RA agonist ATRA seemed to influence fibronectin deposition, however only at higher concentrations suggesting toxic effects and/or a lack of a critical role RA signaling has on this process. Collagen synthesis persisted, suggesting modulation of collagen synthesis is not linked to RA signaling. Further work is needed to elucidate the specifics of RA signaling within the TM.

Funding Source: Novartis Institutes for Biomedical Research, NIH-NIGMS

Recommended Citation:
Muniz Becerra, Johnathan ; Wilson , Christopher ; Vollmer , Thomas . "Investigating the role of retinoic acid signaling in modulation of trabecular meshwork matrix" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1679

Effects of Photo modulation on IPSC derive beta cells

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Type 1 diabetic patients face autoimmuno-desctruction to their insulin producing cells, called beta cells, which are located in islets of the pancreas. Islet transplantation eliminates the need for daily insulin injections; however, it includes the disadvantage of patient immune-rejection and insufficient supply of beta cell donors. Human Induced pluripotent stem cell (IPSC s) derived beta cells, are patient specific cell types, that present a potentially unlimited source of pancreatic endocrine lineage cells. Photo Biomodulation (PBM) is the use of red and near infrared light to stimulate cell and tissue growth, and has been reported to increase proliferation and differentiation in different stem cell derived cells. Two beta cell analogs IPSCs, derived and mice extracted, with their respective control groups were exposed to Photo biomodulation therapy. Live imaging, measuring ROS and Calcium concentration, was taken before and, 5 and 10 minutes after exposure. We observed an increase in Calcium and ROS concentration. PBM may have the potential to increase beta cells' insulin production and maturation. The proposed mechanism is based on the Photodissociation of molecule that functions to inhibit oxygen in mitochondrion respiratory chain from primary suspected chromophore Cytochrome C Oxidase. Potential application includes using PBM therapy to prep beta cells derived from IPSCs in transplantation for patients with type 1 diabetes.

Funding Source: NIH-NIGMS

Recommended Citation:
Ordaz, Samantha; Liebman, Calebe; Inyang, Edidiong; Cho, Michael. "Effects of Photo modulation on IPSC derive beta cells" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1651

Chronic Stress Alters Brain Structure and Function: A Focus on the Hippocampus

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The purpose of these studies is to demonstrate the effects of a novel stressor called unpredictable chronic restraint (UCR) on rodents using 1) the Y-maze to analyze spatial memory, 2) hippocampal dendritic complexity to measure neuronal plasticity, and 3) biometrics to determine the effectiveness of UCR. Sprague-Dawley adult rats were placed in wire-mesh restraints and gently shaken (orbital shaker -120-125rpm) for 30 or 60 min/session at different times in 3-6 consecutive days followed by 1-2 days off over three weeks. In the Y-maze (4-hr delay), UCR impaired spatial memory in males when no changes were observed in females: UCR males entered and spent similar amounts of time in the novel and other arms, whereas UCR females entered and spent more time in the novel arm versus the other arm. Total entries in the Y-maze during exploration were similar among groups, demonstrating that motivation was alike. Quantification of dendritic arbor complexity of CA3 hippocampal neurons is currently ongoing but will be illustrated with our Sholl and branch point measures. In a separate study, chronic restraint reduced body weight gain in both sexes decreased thymus weight in males and lowered uterine weight in females. Chronic stress did not alter adrenal weight in both sexes. Thus far, this work exhibits UCR to impair spatial memory in male rats, whereas females remain intact. UCR's impact on the hippocampal structure is ongoing, but both the Y-maze results and the biometrics suggest that UCR may be an effective chronic stressor paradigm for male rats.

Funding Source: NIH-NIGMS

Recommended Citation:
Parada, Priscilla; Peay, Dylan; Conrad, Cheryl. "Chronic Stress Alters Brain Structure and Function: A Focus on the Hippocampus" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1647

Cognitive Variability and Brain Aging in Late-Life Depression

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Background: Dispersion across cognitive test scores, a measure of variability in cognitive performance, may be an indication of pathological aging. The aim of the current study was to investigate the association of test dispersion with structural brain variables and cognitive decline in non-demented older adults with major depression (MD) and healthy controls (HC). We hypothesized that those with greater dispersion would have lower hippocampal volumes (HPC) and higher white matter hypointensities (WMH) and that dispersion would predict cognitive decline at one-year follow-up.

Methods: Subjects included 121 MD and 39 HC subjects who participated in the NBOLD study at UConn Health. Inclusion criteria were age 60+ and a psychiatrist's diagnosis of MD for the patient group. Dementia and other major neuropsychiatric illnesses were exclusion criteria. Dispersion was calculated as the standard deviation of z-scores divided by group mean z-scores of a demographically adjusted neuropsychological test performance across a comprehensive battery.

Results: Dispersion positively correlated with WMH in both HC (r=0.386; p =.001) and MD (r=0.318; p=0.001), and negatively correlated with left HPC volume in MD (r=-0.191; p=0.034). Linear regression analyses accounting for baseline cognitive performance, demographics, and depression found that dispersion predicted cognitive tasks performance at a year follow up. For older adults with MD word list (WL) 1-3 (p=.038), WL delayed recall (DR) (p=.020) and symbol digit modality test (SDMT) (p=.035) were predictors. For HC, dispersion was predicted for logical memory (LM) DR (p=.004) and Benton test (p=.003).

Conclusions: Dispersion is correlated with evidence of brain aging in older adults with MD. Future studies may look at ways to reduce dispersion in older adults and help prevent cognitive decline.

Funding Source: NIH-NIGMS, CICATS, Educational and research grant from the Leo and Anne Albert Charitable Trust

Spatial and developmental mapping of choroid plexus macrophages in a maternal immune activation (MIA) model

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The choroid plexus secretes cerebral spinal fluid (CSF) which has been shown to regulate brain development, homeostasis, and disease. In addition, previous studies have demonstrated that the choroid plexus functions as the blood-CSF barrier to gate immune cell entry into the central nervous system (CNS) and orchestrates immune cell entry in multiple disease models (such as spinal cord injury and experimental autoimmune encephalomyelitis). Perturbations in the maternal immune system may alter the normal development of the fetus and can lead to neurodevelopmental diseases such as autism spectrum disorder (ASD). Published work has shown that the brain's immune environment and its microglial population are altered in ASD patients. Animal models demonstrate that maternal immune activation (MIA) can trigger neurodevelopmental changes and altered behaviors in offspring. However, how choroid plexus macrophages develop, if the population undergo changes in neurodevelopmental disease models, and how the altered choroid plexus function may affect cortical development in models such as MIA remains to be studied. Thus, in this study, we compared baseline microglia cell numbers in different anatomical structures and time points throughout development. In addition, we analyzed the choroid plexus macrophages in the saline (control) or PolyI:C (MIA) injected mice by histology. Together, preliminary results show that MIA treatment results in distribution and morphology changes in choroid plexus macrophages.

Funding Source: Simons Foundation Autism Research Initiative (SFARI), the Division of Medical Sciences at Harvard Medical School, NIH R01 NS088566, NIH T32 , The New York Stem Cell Foundation, and NIH-NIGMS

The Effects of Vagal Nerve Stimulation on Degeneration of the Substantia Nigra in a Rat Model of Parkinson's Disease

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Vagus nerve stimulation (VNS) has been used to treat depression and epilepsy and is thought to act by upregulating growth factors in several brain areas. The upregulation of growth factors might serve to reduce the loss of neurons in Parkinson's disease (PD). We investigated the effects of VNS on degeneration of the substantia nigra (SNR) in a rat model of PD. Seventeen male rats were randomly assigned to one of three treatment conditions: Control, PD, and PD+VNS. PD animals received an injection of 6-hydroxydopamine (6-OHDA) into the left medial forebrain bundle. PD+VNS animals received a similar injection but then also had a small cuff electrode implanted over the left vagus nerve. One week post injection, the PD+VNS animals received 30 minutes of VNS each day for one week after which all animals were perfused and the brains cryosectioned. Sections were immunohistochemically stained for tyrosine hydroxylase (TH). All TH positive cells were counted on the left and right SNR. Cell loss was estimated as the number of TH positive cells on the left divided by the number of cells on the right. The results showed that all animals receiving 6-OHDA showed a significantly reduced number of TH positive neurons compared to controls. The PD animals showed a 50% reduction and the PD+VNS showed a 60% reduction. There were no significant differences between animals receiving VNS and those that did not. Vagal nerve stimulation did not reduce the loss of neurons within the SNR following medial forebrain bundle injections of 6-OHDA.

Funding Source: School of Biological and Health Systems Engineering at Arizona State University, NIH-NIGMS

Gain-of –Function Mutation in Beclin 1 Mitigates Acute Kidney Injury Through Autophagy Activation in Mice

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Acute kidney injury (AKI) is a specific disease that results with in-hospital complications. This disease leads to high mortality and morbidity rates which may result in chronic kidney disease with dialysis dependence or even death. Autophagy is an important mechanism for ridding the cell of injured or unwanted cytoplasmic constituents and for degrading normal components in response to energy needs. It has proved to participate in renal repair and to alleviate AKI. Beclin 1 is a gene that facilitates and regulates autophagy levels. It is responsible for recruiting proteins necessary for the construction of the autophagosome core, which is vital for autophagy. It is also known to contain a Bcl-2 binding domain. Bcl-2 is another protein that is vital for the regulation of autophagy and acts as an antagonist. When Bcl-2 binds to Beclin 1, a complex is formed that ultimately disrupts Beclin 1's autophagy function. In the absence of Bcl-2 binding, Beclin 1 mutants induce excessive autophagy. The goal of this research project is to determine if gain-of function of Beclin 1 mutation increases autophagy in the kidney and attenuates AKI. In order to do this, mutant Beclin 1 Knock-in mice (BK) underwent Ischemia Reperfusion Injury (IRI) in order to simulate AKI. Kidney tissue was harvested and then tested. Western blot was used to calculate levels of specific autophagy marker proteins. Serum creatinine and blood urea nitrogen levels were also tested. Lastly, Hematoxylin & Eosin (HE) and Periodic Acid-Schiff (PAS) staining were used to evaluate kidney histology.

Funding Source: NIH-NIGMS

A Real-Time Model-Driven Diagnostic and Therapeutic Evaluation of Patients at Risk of Acute Kidney Injury: A Pilot Study

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Acute Kidney Injury (AKI) is a frequently diagnosed form of kidney disease in hospitalized patients. Although serum creatinine is a primary indicator of kidney function, it is a late marker of AKI because it lags behind decreases in Glomerular Filtration Rate (GFR). This is a major cause of delayed AKI diagnoses. For this reason, we developed a time-updated AKI prognostic model and integrated it into the Electronic Health Record (EHR) of the Yale New-Haven Hospital. The model generated a "Pre-AKI Alert" that notified study personnel when a hospitalized patient exhibited a >30% risk of developing AKI in the near future. Each patient (n=59) was monitored for three days via urine and blood sample collection and EHR examination to check for the development of creatinine-defined AKI. Of the 59 inpatients enrolled, 12 (20%) developed AKI within the next 48 hours post-alert and 7 (12%) died during the hospitalization and 12% received a nephrotoxic medication within 24-hours of the alert. 25% of patients who developed AKI had a MABP < 65 at the time of pre-AKI alert compared to 6% percent of patients who did not develop AKI (p=0.092). 75% of patients who developed AKI had urine hyaline casts at the time of pre-AKI alert compared to 26% of those who did not develop AKI (p=0.002). In conclusion, some patients at high risk of AKI nevertheless receive nephrotoxic medications. The prevalence of hyaline casts among those who developed AKI suggests that IV fluid administration may be a therapeutic option in this population.

Funding Source: NIH-NIDDK, NIH-NIGMS

Recommended Citation:
Vela, Jr., Ricardo; Wilson, F. Perry; Ugwuowo, Ugochukwu. "A Real-Time Model-Driven Diagnostic and Therapeutic Evaluation of Patients at Risk of Acute Kidney Injury: A Pilot Study" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1658

Environmental Health 1

Powder Metal Combustion in a Counter-Flow Burner and Hele-Shaw Cell

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The world is in dire need of an efficient zero-carbon energy carrier. The utilization of fossil fuels releases millions of tons of carbon into the atmosphere every year, which has horrible repercussions around the globe. Metal powders can be utilized in combustion and then recycled utilizing green renewable energy. It is possible to sustain a circular economy in which metal fuels power the world without damaging the environment. The combustion properties of these metal powders have not been modeled scientifically for efficient engine design. The construction of a counterflow burner with the capacity of preheating an air-metal powder mixture is necessary for the quantification of burning velocity in relationship to initial temperature. The counterflow burner is the next iteration of several testing apparatus currently being utilized. The design has a longer nozzle for a more laminar flow, several pre-heating elements, and an updated powder dispersion system. The Hele-Shaw cell consists of two transparent parallel plates in which a fluid flow allows for the propagation of a metal suspension flame. The data acquisition utilized in the experiments with the Hele-Shaw cell requires the development of video-recognition software capable of tracking the front of the flame, the size and number of instabilities, and the brightness in each frame. By utilizing these two methodologies, it is possible to further model and understand the combustion properties of metal flames.

Funding Source: NIH-NIGMS, NSF, UTEP, McGill

Recommended Citation:
Aranda, Luis; Blais, Frederic; Palecka, Jan; Bergthorson, Jeffrey. "Powder Metal Combustion in a Counter-Flow Burner and Hele-Shaw Cell" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1619

Contamination of Candies made from Plants that can be used for Phytoremediation of Toxic Metals

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Millions of children are exposed to lead leading to neurological damage, slowed growth and development, as well as learning and behavior problems. The CDC has determined that there is no information about safe blood lead levels. Some of the exposure to lead in these young children have been documented as related to the consumption of candies. Some candies are made from tamarind pulp and sugar which is well known as Mexican candy. The tamarind tree has also been researched as a phytoremediator of soil as well as air. Studies have shown that peanut plants tend to accumulate lead and are feasible for phytoremediation. The objective of this project is to test candies made from tamarind and peanuts plants bought in El Paso, TX and Juarez, Mexico. The candies used where "Mazapan", "Pulparindo", and "Tam y Toon". Two types of candies were purchased from a candy store in Juarez; "Mazapan" (sample 2) and "Tam y Toon". In El Paso the candies "Mazapan" (sample 3) and "Pulparindo" were purchased from a candy store located downtown. The Hach system was used to analyze our samples for preliminary results of trace levels of lead. The Hach system has a sensitivity range of 0.1ppm -2ppm. The results were compared using ICP-OES. The ICP-OES has a higher sensitivity to trace levels of metals. It can detect ppb levels. Our results show that the Hach System was able to detect levels as high as 0.03 ppm in the tamarind candies. The results for the "Mazapan" were negligible. The ICP-OES detected higher levels in both kinds of candies. The Tamarind candies from Mexico had 17.71 ppm and the Tamarind candy from El Paso had 11.15 ppm. The Mazapan candy from El Paso had -0.067 ppm and the Mazapan from El Paso had 0.26. Our results indicate that candies made from plants that are phyto-remediators contain toxic amounts of Lead.

Recommended Citation:
Hernandez, Celeste; Alvarez, Paola; Flores, Raymond; Arteaga, Maria. "Contamination of Candies made from Plants that can be used for Phytoremediation of Toxic Metals" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1705

Identifying and Comparing Pathogens found in Spices obtained from Major Food Companies and those from Smaller International Supermarkets

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The purpose of our research is to identify pathogens in spices from major food companies and compare these to pathogens present in spices purchased from small international food markets. Prior studies have shown that spices may contain filth and pathogenic bacteria due to the fact that most spices in the United States must be imported. In the past, processing of these spices may have allowed for the introduction of pathogens into spices. We predict that spices from small international markets will contain more pathogenic bacteria and filth than the spices from bigger spice suppliers, which introduce a pathogen reduction step prior to the sale of spices, and which we expect will have fewer pathogenic species of bacteria than spices from smaller spice suppliers that may omit this step. To conduct our study, the spices were sifted and placed into a sterile saline solution. Samples were streaked for isolation onto TSA plates and incubated for another 24 hours. Colonies were Gram stained and then identified using the MicroScan autoSCAN4 and to determine their antibiotic resistance profiles. This showed that the spices from international supermarkets contained more pathogens compared to the spices from a larger spice distributor. The spices from the international store had a total of 6 isolates which included S. sciuri, K. puenomiae, S. schleiferi subspecies coagulans, P. agglomerans, and S. schleif-Schlf. These bacteria are known to cause nosocomial infections. The spices from major spice suppliers had 6 isolates as well but weren't as pathogenic. The bacteria identified from the larger spice companies included Micro/Rep spp., S. epidermidis, and S.auricularis. These bacteria are found naturally as part of the human flora.

Recommended Citation:
Skull, Abriyah; Rodriguez, Maximilian; Rico, Oscar; Mendoza, Jose; Chianelli, Xiomara. "Identifying and Comparing Pathogens found in Spices obtained from Major Food Companies and those from Smaller International Supermarkets" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1706

Design of Model Proteins for Studying the Kinetics of Split Intein Gp41-1

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Misfolded proteins that adopt amyloid conformations are known to play pathological roles in neurodegenerative diseases. Many of those large amyloids suffer from chemical shift degeneracy and thus pose a challenge in structural elucidation at the atomic level by solid-state Nuclear Magnetic Resonance (NMR). Segmental isotopic labeling of proteins using a split intein technique reduces this degeneracy by rendering only a small region of the intact protein NMR-visible. Split inteins are two halves of a functional protein that can natively trans-splice two separate polypeptides together, forming a peptide bond and excising themselves out of the sequence. However, in order to employ such a tool, there must be an understanding of the biochemical and biophysical properties of these inteins. Here, we designed model proteins to study the properties of the split inteins Cfa-1 and Gp41-1 focusing specifically on the split junction, the amino acid sequence found in the interface between the intein C-terminal and the adjoining polypeptide, which determines the kinetics and properties of split inteins. Their properties were studied using either Green Fluorescent Protein (GFP) or Yellow Fluorescent Protein (YFP) tagged constructs to investigate their rates of ligation by comparing SDS-PAGE band intensities and molecular weight shifts. This tool will be used in conjunction with a screening of various split junctions in order to design model proteins and develop a library of split junction sequences with their characteristic properties. This library can become an essential tool for the structural studies of large amyloids as well as other large dynamic proteins.

Funding Source: NIH-NIGMS

Recommended Citation:
Zavala, Gerardo; Madrid, Carla; Nguyen, Thuy; Reynolds, Kimberly; Frederick, Kendra. "Design of Model Proteins for Studying the Kinetics of Split Intein Gp41-1" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1692

Health Disparities 1

Public Image Control: The Effects of Diversity Trainer Characteristics on Diversity Training Reactions

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According to past studies the increased diversity of the U.S. workforce presents both a challenge and an opportunity for organizations. Organizations are increasingly turning to diversity training to address these concerns and to attempt to realize the full benefits of an increasingly diverse employee population. However, there is little research on whether physical characteristics of the diversity trainer can influence how much trainees learn. 282 participants participated in a study utilizing a 3 x 3 between person experimental design to examine the effects of trainer race (two White trainers, two Black trainers, or a White trainer and Black trainer) and gender (two male trainers, two female trainers, or a male and a female trainer) on the ability to retain diversity training information, as well attitudes towards the training and trainers, after a short online diversity training. Female trainers were more likely to impact organizational message and be perceived as more credible than male trainers or a mixed gender pair. Furthermore, the results show an interaction such that that non-White participants preferred having Black trainers for diversity training as opposed to White participants who preferred White trainers. However, all participants thought there would be greater potential backlash if the trainers were Black. This study provides important insights into how trainees react to diversity training on the basis of trainer characteristics. Implications and future directions of this research are discussed.

Funding Source: NIH-NIGMS, BUILDing SCHOLARS

The Deficiencies of the Healthcare Industry in Mexico for Prosthetic Limb Recipients

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Being a prosthetic limb recipient in Mexico is not easy. Although being the recipient of a prosthetic limb generally leads to improvement in optimism, mobility, and independence, recipients with prostheses must deal with a vast array of obstacles in their lives. These include discrimination, limited transportation, unsuitable infrastructure, and deficiencies in the healthcare industry. In particular, the aim of this study is to examine the obstacles faced by prosthetic limb recipients when dealing with the Mexican healthcare system. This research uses a mixed-method approach to gain an understanding of the deficiencies experienced by prosthetic limb recipients. Research was conducted in four sites throughout Mexico: Oaxaca, Guadalajara, Mexico City, and Cuernavaca, to explore the experiences of prosthetic limb recipients. Interviews were conducted with prosthetic limb recipients, their family members, and physical therapists. Preliminary findings show that the medical sector is lacking in the healthcare it provides its patients. For example, instances of medical negligence, corruption, shortage of medicine, and discrimination were noted by participants. This project aims to raise awareness of the deficiencies of the healthcare industry in Mexico, and offer a possible approach to solve them, or at the very least, address them to representatives of the healthcare industry in Mexico.

Funding Source: LIMBS International, NIH_NIGMS

Recommended Citation:
Armendariz, Sergio; Cordero, Katarina; Williams, Rachel; Renteria, Roger; Murga, Aurelia. "The Deficiencies of the Healthcare Industry in Mexico for Prosthetic Limb Recipients" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1623

The Impact of Intra-Familial Separation and Reunification on Educational Attainment Levels Among Mexican Immigrant Children

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Immigrant children experiencing familial separation and reunification are more likely to develop psychological disorders such as toxic stress and anxiety. Further, these children exhibit increased behavioral issues as reunified families adjust to changes in family dynamics. Literature suggests the effects of immigration related familial separation and reunification on the mental, physical, and behavioral health of children could be associated with lower educational outcomes. Therefore, the purpose of this study is to investigate the impact of familial separation and reunification on educational attainment among Mexican immigrant children. It is hypothesized that familial separation will be negatively associated with educational attainment among Mexican immigrant children compared to Mexican immigrant children who are never separated. The cross-sectional study utilizes data from the American Community Survey over a 5-year period (2011-2016). Statistical analyses suggest familial separation and reunification negatively impacts educational attainment. Separated Mexican immigrant children exhibit significantly lower rates of educational attainment. The findings further demonstrate that Mexican immigrant girls and boys who experienced separation and reunification are significantly more likely to be behind their peers in schooling. However, Mexican immigrant boys who were separated and reunified experience the greatest impact. Future work should explore long-term implications of separation and reunification on educational outcomes of Mexican immigrant children. Because educational attainment directly impacts quality of life, it is imperative to mitigate factors that impede educational attainment among this population.

Funding Source: NIH-NIGMS, Robert Wood Johnson Foundation Center for Health Policy at the University of New Mexico

Recommended Citation:
Chacon, Lauren; Cartwright, Kate. "The Impact of Intra-Familial Separation and Reunification on Educational Attainment Levels Among Mexican Immigrant Children" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1667

The effect of ethnic-based prejudice on working memory and anxiety

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Background. Experiencing prejudice can have negative health implications. Research shows that experiencing prejudice is correlated with increased self-reported levels of anxiety and impairments in working memory. The present experiment tests how prejudice affects anxiety and working memory. Resilience is explored as a protective factor. Methods. A total of 36 Latinx students were recruited to participate in this experiment. Participants were randomly assigned to a prejudice versus no prejudice condition. Before receiving the experimental condition, participants: (a) were instructed to complete a demographic questionnaire, the State-trait anxiety inventory (STAI), the Brief Resilience Scale and, (b) heart rate was recorded as the physiological measure of anxiety. After interacting with a prejudiced (or non-prejudiced) individual, the participant's heart rate was recorded a second time, completed two working memory tasks, and a post-STAI. Results. Participants' heart rate increased 10 beats per minute and increased 7 points in the STAI scale in the prejudice condition. In contrast, participants in the no prejudice condition exhibited a 2 beats per minute increase in heart rate and 1 point increase in the STAI scale. Heart rate and self-reported anxiety differed between conditions. Resilience was negatively correlated with post STAI, such that participants in the prejudice condition who were high in resilience expressed less anxiety. Conclusion. The present study addressed the gap in the literature regarding experimental investigations of the interaction between resilience and discrimination as it relates to anxiety and in turn, the health of Latinxs.

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Ayuda de Súper Mamá: Using Intervention Mapping to Develop a Video Text Message Educational Program to increase HPV vaccination in Hispanic Adolescents

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This study was designed to create a theory-based, Spanish language multimedia messaging service (MMS) educational program for Hispanic mothers. This program focuses on increasing human papillomavirus (HPV) vaccination rates in Hispanic youth and was developed using intervention mapping. Intervention mapping uses six steps and involves: conducting a needs assessment, identifying outcomes and objectives, selecting methods and strategies, program production, program implementation, and evaluation. During Step 1 we conducted a needs assessment based on the Integrative Model of Behavioral Prediction (IM) to identify mothers' decisions to vaccinate their child. A qualitative and quantitative study were conducted to assess the needs of this population. For the qualitative study, we conducted 85 in-depth interviews, and for the prospective study, we surveyed 332 mothers with an adolescent child aged 11-17. The qualitative study resulted in a list of salient beliefs. The findings of the quantitative study allowed us to refine the list of salient beliefs. We found that norms, attitudes, and self-efficacy were correlated with the intention to vaccinate. Step 2 of the process resulted in the development of 11 performance objectives and 10 determinants. During Step 3, we identified methods and strategies that would be effective. The educational program consists of 40 short animated videos that will be sent through MMS messaging service. Once the program is fully completed it will be implemented and evaluated. The use of this method of intervention has the potential to expand access to health care information with populations with barriers to accessing health care.

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Eating, Depression and Gaining Weight

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Previous literature has shown binge eating and depression have a bidirectional relationship. However, there is a lack of literature that examines potential variables that may help explain this relationship. This study will examine emotional eating as a potential variable that is associated with depression and weight gain. We hypothesized that among high emotional eaters, percent body fat will increase significantly as negative affect increases, when compared to low emotional eaters whose percent body fat will increase less as negative affect increases. The participants consisted of 183 ASU undergraduate students. They completed an online questionnaire on Qualtrics. Body fat percent was assessed using a body impedance assessment machine. Positive and Negative Affect Schedule was used to access for depression and the Motivation for Eating Scale to measure emotional eating. The overall regression equation, which included the two-way interactions among the three variables, was also significant [$F(6,147) = 14.54$; $p < .01$]. None of the two way interactions were significant: Gender and Negative Affect [$t(153) = .405$; $p=.686$] , Gender and Emotional Eating [$t(153) = -1.824$; $p=.070$] ,and Negative Affect and Emotional Eating [$t(153) =.134$; $p=.893$]. Negative affect did not explain the variance accounted for on percent body fat scores. This could be due to the lack of representative population that was used in the study. When looking at the race distribution in the study, it did not represented the population of either the undergrads at ASU or the Phoenix area.

Funding Source: NIH-NIGMS

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Promoting Hispanic health via community health workers and motivational interviewing

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Hispanics in the United States have less access to quality health care. By providing information regarding preventative measures and disease management, Community Health Workers (CHW) can help community members navigate the healthcare system and address their distrust of healthcare professionals. Previous literature indicates that interventions using motivational interventions (MI) help bring awareness to risky behaviors and increase the chances that a person will make healthy behavioral changes. This study aimed to investigate the effectiveness of an intervention where CHWs conduct motivational interviews for healthy lifestyle changes. This project further aimed to examine the perceived barriers and benefits of healthy behavioral change among a Hispanic population. It was hypothesized that physical body changes, such as weight and blood pressure, would differ significantly between those who received MI and those who did not. The study used baseline and follow-up data from the Healthy Fit program. To test our hypothesis, we compared the body measurements and reported behavioral changes between program participants who received MI and those participants who did not receive MI using t-tests. Results indicate that participants receiving MI lost more weight than participants not receiving MI but did not have significantly different changes in blood pressure. These findings suggest that MI may be more effective in helping individuals address healthy behavioral changes. Qualitative analyses identified personal health and family as main motivators for change. Future interventions may benefit from emphasizing these change motivators.

Funding Source: NIH-NIGMS, El Paso Public Health Department

Recommended Citation:
Portillo, Erin; Vasquez, Denise; Brown, Louis. "Promoting Hispanic health via community health workers and motivational interviewing" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1690

Infectious Diseases 1

Candida albicans strains CHN1 and 529L Colonize the Murine Gastrointestinal Tract in the Absence of Antibiotic Pre-Treatment

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Candida albicans (CA), the most common human fungal pathogen, colonizes the gastrointestinal tract (GI) of 40-80% of humans. Mice, however, are resistant to CA GI colonization unless pre-treated with oral antibiotics. Our group has shown that specific bacterial gut microbiota are essential for maintaining CA GI colonization resistance. Previous studies showing that mice are resistant to CA GI colonization have only used the laboratory strain SC5314. We hypothesized that CA clinical isolates may be able to colonize the murine GI tract in the absence of antibiotics. C3H/HeN mice (female, 6-8 wks, Envigo, n=8 per group) were orally gavaged with $2x10^8$ cfu CA. The following CA strains were used: 1) laboratory strain SC5314; 2) Can092; 3) 529L; 4) CHN1. Fecal samples were collected weekly for colonization levels by culturing stool homogenates on selective media. Stool was also collected for genomic DNA. CA in vitro growth curves were assessed in YPD media grown aerobically at 30ºC. CA strains CHN1 and 529L sustainably colonized the murine GI tract in the absence of antibiotics, whereas strains SC5314 and Can092 did not. Furthermore, the in vitro aerobic growth curves of the four CA strains tested did not differ significantly (two way Anova). Specific strains of Candida albicans can colonize the gastrointestinal tract of mice without the use of antibiotics. GI colonizing ability is not correlated with in vitro growth. Future studies will attempt to dissect genomic and transcriptomic differences between colonizing and non-colonizing CA strains.

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Molecular imprinted polymers with West Nile antibody templates

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Molecular imprinting is a technology in which silane monomers are fixed by rapid polymerization around a template molecule. Removal of the template molecule leaves a molecular imprinted polymer (MIP) with active sites that can bind specifically to the template molecule. The aim of this study was to develop MIP reagents capable of binding specifically to West Nile antibodies (WNA). WNA were obtained and purified by affinity chromatography of serum obtained from mice infected with West Nile virus. The MIPs were synthesized by mixing millimolar concenrations of the monomers tetraethyl orthosilicate, 3-aminopropyl triethoxysilane, carboxybutyl 3-amidepropyl triethoxysilane, and octyl triethoxysilane in ethanol, carbon black, and a 50 mM HEPES, 100mM NaCl buffer, and approximately 200 μg/ml West Nile antibodies. The solution was adjusted to a pH of 7.4 ± 0.2 and left at room temperature for three days to complete the reaction. The WNA were removed from the MIPs by washing the particles with elution buffer three times and two additional times with HEPES. A fluorescent immunoassay was performed using the synthesized MIPs in a high bind 96 well plate previously incubated with WNA and BSA as the positive and negative samples. The results obtained through confocal imaging showed a high number of the imprinted particles attached to the wells onto which WNA was adsorbed, while only a few remained attached on the other wells. This shows WNA MIPs bound specifically to its template and suggest that MIP technology could be used to develop an alternative to antibody-based diagnostics.

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Searching for the Elusive Mycoplasma pneumoniae Vaccine

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Mycoplasma pneumoniae is a human pathogen that causes upper and lower respiratory tract infections and accounts for about 40% of all cases of community acquired pneumonia. It is estimated that M. pneumoniae infection results in 100,000 hospitalizations annually in the US alone, with approximately 2 million total cases of infection occurring every year. M. pneumoniae has been shown to cause a wide array of extrapulmonary infections, and some studies suggest that infected individuals can develop asthma. Unfortunately, M. pneumoniae infections are often not diagnosed or treated correctly. Furthermore, M. pneumoniae has developed resistance to previously effective macrolide antibiotics, further complicating the successful treatment of the disease, thus highlighting the importance of developing a safe and efficacious vaccine. Efficacious vaccines against M. pneumoniae have proven elusive, however, as past vaccination attempts actually exacerbated disease in some recipients that were subsequently exposed to M. pneumoniae. It is now known that M. pneumoniae expresses a unique and recently discovered ADP-ribosylating vacuolating cytotoxin called Community-Acquired Respiratory Distress Syndrome (CARDS) toxin that causes hyper-inflammation, cytopathology, and exacerbation of asthma by causing a Th_2 type, allergic immune response. We hypothesize that CARDS toxin is the responsible factor for vaccine-induced disease exacerbation and that a CARDS deficient mutant can be a key candidate in developing a vaccine. Herein we describe the screening of 1650 M. pneumoniae mutants generated via haystack mutagenesis and the identification of a potential CARDS deficient mutant. This mutant will be tested as a vaccine candidate in future experiments in an experimental mouse model.

Funding Source: NIH-NIGMS

NKT cell-controlled reduction of inflammation due to the regulation of Cytokines

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Our immune system is supposed to be our body's defense, but what happens if it is turned against us? The bacterium Francisella tularensis (Francisella) is a pathogen which triggers an overactive pro-inflammatory response of the body's immune system which leads to the death of the host. During in vivo experimentation mice succumbing to Francisella infection developed a high pro-inflammatory cytokine response as measured by serum cytokine analysis compared with a mild response in mice surviving the infection. Therefore, we hypothesized that reducing the pro-inflammatory response could prevent death. Natural Killer T (NKT) cells are a subset of leukocyte with regulatory and pro-inflammatory functions that potentially could control the overactive immune response. Indeed, mice lacking NKT cells are more prone to disease and were observed to have a higher cytokine response than mice sufficient in NKT cells. This shows a regulatory role for NKT cells in controlling the infection and reducing the cytokine response, thereby reducing lethality. In addition, in vitro experiments have shown that purified NKT cells can directly suppress the inflammation caused by infected macrophages. Furthermore, two types of NKT cells (type I and type II) exist which have opposing roles in regulating the cytokine response. Current experiments will separately analyze the role of type I and type II NKT cells in regulating the inflammatory response to Francisella. Knowing this, therapies can be developed that target the appropriate subset of NKT cells to reduce the overactive pro-inflammatory responses that cause death and disease.

Funding Source: NIH-NIGMS

Translational Biomedicine 1

Three Dimensional printed polycaprolactone scaffolds for meniscus injury repair.

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Meniscus can absorb the shock the stress between the articular cartilage in the knee. Damages are induced due to old age or meniscus tearing from athletic players. These damages can be treated using partial meniscectomy, cell-based meniscus repair and tissue regeneration. In our study, PCL was used to be as a matrix material for meniscus replacement using 3D printing, and the scaffold mechanics was measured and modeled using the Finite Element Analysis (FEA). We optimized the parameters of PCL printing from infill percentage, patterns, the extrusion rate, and the temperature and the pressure. The optimal parameters included the temperature at 61°C, pressure at 250 kPa, 40% infill, 1.5 mm/s extrusion rate, layer height of 0.15mm, and a hexagonal pattern in terms of current results. . Then the FEA was used to simulate the printed PCL scaffold status as an artificial replacement when walking and standing normally. When analyzing the data for the FEA, it has shown that even with a safety measure that PCL is a bad artificial replacement even for a short term. These above results conclude that the current structure of printed PCL scaffold needs further improvement in the material itself as well as the infill patterns.

Funding Source: NIH-NIGMS

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LigandNet: A Machine-Learning Based Toolkit for Predicting Ligand Activity to Proteins

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LigandNet is a Machine Learning (ML) toolbox that combines different ligand-based models into an open source platform that can predict if a ligand may have an activity to a specific protein. Finding a ligand that will bind to a human protein and have a significant signaling effect through the cell can be an expensive task. Currently, ML models are being employed throughout many scientific fields and are being successfully applied to drug discovery research. In this project, we have applied advanced ML approaches such as Random Forest (RF), Support Vector Machine (SVM), Linear Regression (LR), Extra Tree Classifier (ETC) and Deep Learning (DL) to classify the ligands as active/binder or inactive/nonbinder. We obtained the known active ligands for each of 1704 proteins from the Pharos (pharos.nih.gov) database. For each of the known active ligands, decoys were generated using DecoyFinder (http://urvnutrigenomica-ctns.github.io/DecoyFinder/) and Zinc database (http://zinc.docking.org/). ML models were developed for each of the protein-ligand sets by using known actives and generated decoys. ECFP6 fingerprints and Topological Pharmacophore Atomic Triplet Fingerprint (TPATF) from MayaChemTools (http://www.mayachemtools.org/) were employed as feature generators in developing the models. Models were validated using highest positive predictive value (PPV), sensitivity, and area under the curve of the receiver operating characteristic plots (ROC-AUC) to determine which model works best with each dataset of the proteins, determining the accuracy and precision of each ML approach. The developed models are available on GitHub (https://github.com/sirimullalab/LigandNet).

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Localizing Perinuclear Ribosome-Protected mRNAs in Mammalian Cells

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Gene sequencing has become a main focus in research laboratories. Understanding the order of nucleotides within a DNA molecule can provide a better explanation for the phenotypes seen on a subject. Though gene sequencing is a broad spectrum technique, this project has focused on ribosome profiling and RNA-sequencing which are used to determine the translational rates of a cell as well as the position of the constituents. This type of sequencing can profile actively translated mRNA from different regions in the same cell. This project revolved around locating ribosomes that were believed to be at the perinuclear membrane and stripping off these ribosomes for further sequencing. Through the use of a nuclei isolation protocol it was shown that ribosomes are present at the perinuclear membrane. Following this discovery, a detergent-based protocol was followed and after optimizing it, the next step would be to profile the ribosomes found at this location. These standardized protocols can be applied for identifying actively translating mRNAs that could potentially lead to diseases which in turn would lead to early treatment and/or prevention.

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Immunohistochemical localization of vasoactive intestinal polypeptide in the prefrontal cortex within the rat brain

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A major goal of the UTEP Systems Neuroscience Laboratory is to understand how prefrontal cortical (PFC) circuits help control motivated behaviors through their interactions with the hypothalamus. As a step towards achieving this goal, we examined the distributions and organization of three classes of interneurons within the PFC, including one – vasoactive intestinal polypeptide (VIP)-expressing interneurons –which has not been examined at this level of spatial resolution. Three series of rat brain tissue were each stained separately for VIP or two other interneuronal classes expressing either parvalbumin (PV)/somatostatin (SOM). A fourth series was visualized using a Nissl stain and used as the cytoarchitectural basis for compiling images of the other three series. Three rostrocaudal levels of Nissl-stained tissue were parcellated based on the Swanson (2018) atlas (Levels 6, 8, 10) and consulted to determine boundaries of expression for the three interneuron markers. Results indicate that within Level (L) 6, SOM and VIP are seen predominately in the superficial cortical layers (2, 3) and concentrated in the anterior cingulate region. PV+ neurons are the most abundant and evenly dispersed of the three interneuronal classes at L6; and in L8, especially throughout layers 2, 3, 5. At L8 and L10, SOM+ neurons are evenly distributed and are present in all layers except L1. In contrast, VIP+ neurons in L8 and L10 are concentrated within superficial layers and, in L8, are evenly dispersed throughout cortical areas. We conclude that VIP+ neurons are robustly distributed among SOM+ and PV+ interneuron populations in the PFC.

Funding Source: NIH-NIGMS

Fabrication and Characterization of Electrospun CAP-Based Nanofiber Blends for Tissue Engineering Applications

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The advent of nanotechnology has brought more focus on the applications of electrospinning, a method of producing polymer nanofibers through electrostatic manipulation. Many of the promising aspects of electrospun scaffolds include the tunability of the variety of polymers, both natural and synthetic, that can be manipulated to acquire certain properties. Here, we look at polymers Poly-L-lactic acid (PLLA) and Poly(lactic-co-glycolic) acid (PLGA) blended with cellulose acetate phthalate (CAP) in their characterization and function as biocompatible electrospun scaffolds, through viability tests. PLLA and PLGA were both individually mixed in a 1:1 15% w/v CAP solution for electrospinning. 15% CAP w/v was also individually electrospun for comparison. The electrospinning parameters included a 20-gauge needle for all samples, electrospun at 15kV at a rate of 500μL/hr for an average of 8 hours per sample. After electrospinning, samples were characterized through SEM imaging and FTIR spectroscopy. Following characterization techniques, biocompatibility was tested using osteoblast and ADSCs. The mats were seeded and checked for compatibility after the 3-day mark through MC3T3 and live-dead assays. Electrospinning of all polymer solutions resulted in nanofiber mats which were characterized as bead-less and within 500-800nm in diameter, indicating excellent morphology in terms of simulating an ECM microenvironment. The morphology was further characterized with the introduction of osteoblasts cell line seeded on top, with preliminary analyses suggesting a viable substrate on which to proliferate and differentiate on.

Funding Source: NIH-NIGMS

Bacteriophage delivery of nanoparticles to eradicate biofilm buildup

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A distinctive goal of the Environmental Crew and Life Support Systems within NASA is to obtain a 95% recovery rate of water from urine. In doing so, the need for potable water for future shuttle missions to the International Space Station or possibly even Mars would be eliminated, reducing overall cost exponentially. However, a major obstacle preventing increased water recovery is the repeated biofilm buildup occurring within the Urine Processor Assembly of the NASA toilet system.ECLS systems currently do not posses a standard method for treating built up biofilms, despite past research attempts. Rather than expending energy a new revolutionary approach should address the need for an efficient, adaptable, and reliable biofilm treatment. A technique employing the usage of bacteriophages as a delivery system coupled with magnetic nanoparticles and RF heating to disrupt biofilm buildup was investigated as a viable biofilm treatment. In the proposed technique, low cost and expendable polyvalent bacteriophages would act in targeting the dominant bacteria species initiating surface colonization of the biofilm. With the combined usage of magnetic nanoparticles, the bacteriophages will be able to penetrate biofilm through an applied magnetic force produced by radio frequency heating. The magnetic nanoparticles will then oscillate providing an extra measure of biofilm disruption. Further future applications include researching how the technique fares under microgravity conditions to prove viability for space exploration missions.

Funding Source: NASA, NIH-NIGMS

Quantifying the Shear Modulus of 3D Printed Materials for Use in Foot Orthotics

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Diabetes Mellitus affects over 300 million people globally, with patients often developing diabetic neuropathy. Diabetic neuropathy may result in patients ignoring exposure to excessive mechanical stress or injury. Often times, these risk factors lead to patients experiencing foot ulcers that, if left untreated, increases the possibility for infection and even amputation. Shear force has been identified as a significant foot ulcer generation factor for these patients. The purpose of this study is to use a modified lap shear test to quantify the shear modulus for various 3D printed material for future use in foot orthotics. Seven, 250 mm^2,"Tangoplus" samples were prepared with varying offset angles. Additionally, five, 250 mm^2 samples were prepared with differing composition combinations of "Tangoplus" and "Veroclear", obtaining varying hardness levels. ASTM D3528-96 double lap shear test method by tension loading was used to derive testing setup through the use of an Instron. Shear modulus was then calculated using the tensile load, deformation of the material, and initial dimensions of samples used. The varying material compositions and offset angles created both differing average shear modulus and shear modulus profiles. Through analyzing both sets of data, "Tangoplus" materials with offset angles created a higher resistance to the amount of shear force present and are, therefore, the material most preferred.

Funding Source: NIH-NIGMS

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Synthesis and Functionalization of Fe3O4 magnetic nanoparticles in one step and their potential for medical applications.

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Fe3O4 nanoparticles were synthesized and functionalized successfully by coating them with Poly ethylene glycol in one-step experiment using supercritical conditions of fluids. The synthesis materials used were chosen as they do not confer significant toxicity and thus could be used in vivo. Fe3O4 nanoparticles have been found to be useful in the medical field due to their magnetic properties under applied magnetic field. Based on their large magnetization, Fe3O4 magnetic nanoparticles (MNPs) can agglomerate and behave as one large cluster, which is not required for the biomedical applications. Therefore, the functionalization of MNPs is required to have dispersed particles in the solution and enhance their potential to be used for medical applications such as magnetically induced hyperthermia, magnetic resonance imaging (MRI) and in magnetic targeted drug delivery. We have synthesized functionalized Fe3O4 MNPs by using PEG as surfactant. The morphology and phase structure of the particles were characterized using scanning electron microscope and X-ray diffractometer respectively. The magnetization dependence on temperature was measured for zero-field and field cooling conditions. In order to test the feasibility of the functionalized Fe3O4 MNPs for hyperthermia, the particles were dispersed in distilled water and placed in a coil connected to an AC generator. The coil-generated magnetic field motivates the particles to heat up under Neel and Brown relaxation times. The particles show a good amount of heat presented by specific absorption rate (SAR). To conclude, the results open new root of synthesis functionalized monodispersed Fe3O4 MNPs and their potential for magnetic hyperthermia for cancer treatment.

Funding Source: NIH-NIGMS

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Association between maternal high fat diet, Inflammatory cytokines, and the offspring gut microbiome of primates

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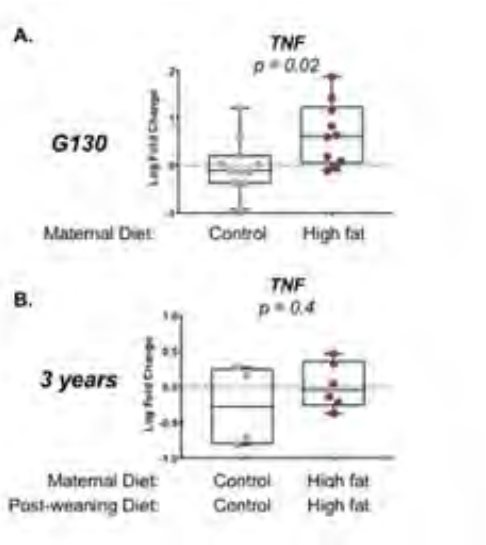
Diet is a strong determinant of the gut microbiome, and our primate model shows that exposure to a maternal high-fat diet (HFD) persistently alters the offspring gut microbiome. However, the role for host factors in modulating these persistent alterations of the microbiome are unclear. To discern the underlying host-microbiome interactions with exposure to maternal HFD, we examined inflammation within the intestine. We hypothesized that maternal HFD is associated with altered expression of inflammatory cytokines in the offspring gut. We used our Japanese macaque model of maternal HFD and obesity where dams consume either a high-fat (36% fat) or a control (14% fat) diet during gestation and lactation. RNA from ascending colon of offspring at gestational day 130 (fetal) and at 3 years (juvenile) was extracted and cDNA was generated. Gene expression analysis was performed by quantitative real-time PCR (qPCR) for TNF and IL-1B with a housekeeping gene. Statistical analysis revealed a significant increase in TNF expression with exposure to a maternal HFD in the fetus (p=0.02, Fig.A), but this increase did not persist to three years of age (p=0.4, Fig.B). IL-1B was not altered in offspring exposed to a maternal HFD when compared to control diet exposed offspring. Altogether, we observe an increase in TNF in the colon with in utero exposure to a maternal HFD. Although this increase was not seen at three years of age, the effects of this in utero exposure may have a persistent impact even after weaning onto a control diet.



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Recommended Citation:
Quinones, Angelica; Prince, Amanda; Aagaard, Kjersti. "Association between maternal high fat diet, Inflammatory cytokines, and the offspring gut microbiome of primates" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1688

Session 2

Addiction 2

Examining the Impact of Training in Motivational Interviewing on Participants' Knowledge, Skills, Intentions, and Attitudes Toward Clients

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Training in Motivational Interviewing (MI), an evidence-based approach to addressing substance abuse, is typically provided in the form of workshops lasting one to three days, which research has found to be insufficient for ensuring skill acquisition. The training model evaluated in this study provided high-quality training in MI to community service providers by incorporating different training components over 23 training hours throughout a 15-week period. A total of 149 participants (70% female) participated in the training; however, only 95 (64%) completed both the Initial and the Booster training. A series of repeated measures ANOVAs were conducted to determine differences in participants' MI knowledge, skills, intentions, and attitudes towards clients. More specifically, we anticipated that there would be increases in each of these across three time points during the training. The results demonstrate that MI Knowledge scores ($F(1.823, 169.524) = 70.232$, $p < 0.0005$) were significantly higher across all times. Moreover, MI skills ($F(1.664, 154.759) = 23.476$, $p < 0.0005$) and attitudes towards clients ($F(1.944, 180.769) = 10.545$, $p < 0.0005$) were significantly higher between times one and times two. However, MI Intentions ($F(1.742, 161.987) = 13.430$, $p < 0.0005$) and attitudes towards clients were significantly lower between times two and times three. Reductions in intentions to use MI and attitudes toward clients was unexpected and inconsistent with the existing evidence. These changes may be predictive of engagement and completion of training which would facilitate implementation of this rigorous, evidence-based training model.

Funding Source: NIH-NIGMS, PDNHF

Cancer 2

The Effects of Herbal Remedies on the Viability of HER-2 Positive Breast Cancer Cell

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Curcumin and Amygdalin are herbal remedies that have been used as cancer treatment alternatives. Curcumin is known as an active ingredient in turmeric and has anti-inflammatory and anti-cancerous properties. Amygdalin, also known as laetrile, is found in the seeds of many fruits (apricots, apples, and bitter almonds) and has also been a popular anti-cancer treatment substance. Our objective is to study the effects of these herbal remedies and the viability of Her2 cells. The curcumin extract was obtained by dissolving a curcumin pill into 96% ethanol. We obtained the amygdalin extract by crushing the apricot pits and mixing with DI water. The solution of each extract was then filtered sterilized and kept in the refrigerator for future use. Cell line 361-P3 Her-2 positive breast cancer cells were cultured in 24-well plate at 1.07 $x10^5$ per well and exposed to curcumin at concentrations ranging from 0.1 mg to 500 mg for 24 hours. In addition, cell line 361-P3 Her-2 positive breast cancer cells were cultured in 24-well plate at 1.01 $x10^5$ per well and exposed to amygdalin at concentrations ranging from 0.3 mg to 300 mg for 24 hours. Cell viability was determined by using Trypan blue dye and cells were counted using the Countess II cell counter. Our results show that as you increase the concentration of curcumin, the cell viability decreased and the IC-50 was 17.01 mg/ml. The results obtained for amygdalin also demonstrate that as you increase the concentration of amygdalin, the cell viability decreased and the IC-50 was 6.809 mg/ml. These results support previous studies reported on the use of curcumin and amygdalin as a potential alternative to traditional cancer treatments.

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Gene Regulation by miRNAs and PRC2 in Glioblastoma Multiforme

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Introduction: Polycomb repressive complex 2 (PRC2), an epigenetic transcriptional regulator, and micro-RNAs (miRNA), RNA molecules that regulate post-transcriptionally, are both important in glioblastoma multiforme (GBM). Preliminary data suggests that PRC2 activates several interferon response pathway genes by repressing miRNAs that target them. How this mechanism impacts interferon response and its role in cancer is unknown.

Methods: The Cancer Genome Atlas (TCGA) was used to analyze pairwise correlations of PRC2 components (EZH2 and SUZ12) to EZH2-activated interferon pathway genes and to test for negative correlation between PRC2 components and EZH2-repressed miRNAs. Lastly, we tested the role of PRC2 on interferon response by examining ISG induction in cells lacking PRC2 components. EZH2-/-, SUZ12-/- and WT GBM cells were treated with IFN-γ. ISG induction was then measured through qRTPCR and immunoblotting.

Results: TCGA mRNA-seq datasets showed most interferon pathway genes were positively correlated with EZH2 expression. Furthermore, a majority of the EZH2-repressed miRNAs were negatively correlated with PRC2. qRTPCR showed EZH2-/- and SUZ12-/- cells treated with IFN-γ have varying levels of ISG induction, while immunoblotting showed pSTAT1 downregulation.

Conclusions: TCGA analysis suggests that indirect activation of interferon pathway genes by PRC2 through miRNA repression likely occurs in solid tumor samples. Effects of PRC2 loss on ISG induction based on qRTPCR so far appears to be inconclusive and highly gene-specific. However, activation of STAT1 through phosphorylation due to IFN-γ treatment showed significant reduction in cells lacking PRC2. This suggests that PRC2 promotes interferon response possibly through activation of interferon pathways genes via miRNAs.

Funding Source: NIH-NIGMS

Recommended Citation:
Gandara, Isaac; Shivram, Haridha; Iyer, Vishwanath. "Gene Regulation by miRNAs and PRC2 in Glioblastoma Multiforme" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1696

Identification of exonic variants for pediatric acute myeloid leukemia at disease diagnosis, remission, and relapse

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Acute myeloid leukemia (AML) is a cancer where myeloblasts cannot mature into healthy white cells. Although patients with AML generally achieve remission following standard induction therapy, almost half of all pediatric AML cases relapse. Precision therapies for pediatric AML are in increasing demand. Whole exome sequencing (WES) data of pediatric AML patients are available in the Therapeutically Applicable Research to Generate Effective Treatment (TARGET) database. From there, we downloaded data of 18 patients between one and 17 years old, where each individual has three WES datasets at three phases: when first diagnosed, in remission following treatment, and after relapse. The objective of the current study is to identify exonic DNA variants from AML patients at these phases. The datasets, ranging from 17 to 31 GB in size in the BAM (binary alignment map) format, are being analyzed using OncoMiner, a web-based bioinformatics pipeline (OncoMiner.utep.edu) for WES data analysis. The first step is to run the OncoMiner Preprocessing program to convert the BAM files to OncoMiner Input files that are then submitted to other OncoMiner modules to assess the variants' deleterious effects and to visualize their distribution on the chromosomes. Finally, a statistical comparison will be conducted to detect any significant differences in the exonic variant profiles among the three time points. While this work is still in progress, we expect the findings will provide insights towards understanding the genetic mechanisms of AML development at the DNA level and help design better strategies for diagnosis and treatment.

Funding Source: NIH-NIGMS

Cell Type Specific Markers in mouse lines to understand P53 in tumor development

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The tumor-suppressor gene p53 is often mutated in cancer cells. The p53 gene encodes a transcription factor that is stabilized and activated in response to DNA damage. Active p53 drives the transcription of target genes (such as p21, a cyclin-dependent kinase inhibitor) that block progression through the cell cycle, allowing repair of the damaged DNA. Activated p53 can also induce expression of proteins that promote apoptosis. Humans with inherited mutations in p53 have a cancer predisposition syndrome termed Li-Fraumeni syndrome. Patients are typically developing specific types of cancers at an early age such as breast cancer, lymphomas, medulloblastomas and soft-tissue sarcomas.

The CRISPR/Cas9 system was used for targeted mutagenesis of p53 in inbred FVB/N embryos. Mice carried mutations in p53 exon 5 (the DNA-binding domain) or deletions in exon 9 (the tetramerization domain) were bred to homozygosity. The lines of mice from Dr. Mary Dickenson's lab included: Flk1-myr-mCherry and Flk1-H2B-YFP (label endothelial cells); NG2-dsRed (label pericytes), SMA-mCherry (label smooth muscle cells), and c-fms-EGFP (label macrophages). Genotyping of mice was done by tail DNA isolation, followed by PCR amplification and agarose gel electrophoresis.

Data show the presence of the marker genes in both homozygous and heterozygous mutant mice. Tumors from the homozygous mice are being analyzed by confocal microscopy and will be used to enrich for different cell types by fluorescence-activated cell sorting (FACS) to explore role(s) of p53 in monitoring (stem) cell differentiation and cellular polarity.

Funding Source: NIH-NIGMS

Recommended Citation:
Rosas, Victoria; Overbeek, Paul; Das, Gokul. "Cell Type Specific Markers in mouse lines to understand P53 in tumor development " (2018). COURI Symposium Abstracts, Fall 2018, ID= 1618

Synthesis of Silver Nanoparticles and Their Effects on Cancer Cells

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In recent years, the use of nanoparticles for therapeutic treatments of cancer has begun to show great promise. The nanoparticles used in this study were composed of silver that were chemically synthesized. Silver is known for its anti-inflammatory and antimicrobial properties. However as a nanoparticle, silver has some anti-cancerous properties. As a treatment, the nanoparticles are localized to the treatment area of the tumor as opposed to most cancer treatments which are systemic. In traditional systemic treatments, the use of the blood stream as a way of delivering the drugs for chemotherapy has many side effects. These side effects include dehydration, malnutrition, and a weakened immune system. Drugs used for chemotherapy target cells that have a high proliferation rate. Since the treatment is systemic, it comes into contact with many body systems that have a fast proliferation rate such as the immune and digestive systems. The damage to the digestive system is caused by the chemotherapy inducing apoptosis cells in the stomach lining, which leads to malnutrition and dehydration as patients are not able to keep down fluids and foods. Also, drugs target the immune system in the patient causing them to become immunosuppressed causing an increased risk of acquiring an infection. However in recent years nanoparticles have emerged as a new experimental treatment option for cancer. Due to the unique surface area to volume ratio only small amounts of the silver nanoparticles need to be used. In this study, the chemically synthesized silver nanoparticles had little amounts of agglomeration and were in the size range needed for therapeutic use. The nanoparticles were then used to treat to HER 2+ breast cancer cells obtained from Dr. Francia's lab at the University of Texas at El Paso. After treatment, the cells were incubated for 24 hours at 37 degrees Celsius with 5% CO_2 levels. All the concentrations of the nanoparticles had a significant effect on the HER 2+ breast cancer cells compared to the negative control.

Recommended Citation:
Zhang, Min Dong; Merino, Jose; Mendoza, Joe; Ballou, Yessenia; Gonzalez Garcia, Diana; Castillo, Karina. "Synthesis of Silver Nanoparticles and Their Effects on Cancer Cells" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1708

Degenerative And Chronic Diseases 2

The relationship between lipedema and Venoarterial Reflex

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Lipedema is an adipose tissue disease in which fluid develops in fat tissue making it painful and persistent; body mass index increases by Stage 1->3. It is hypothesized that lipedema is caused by leaking blood vessels that pool fluid into the lymphatic system, though the mechanism of this behavior is unknown. The purpose of this project was to investigate the Venoarterial Reflex (VAR), a signal veins use to communicate with arteries to control blood flow throughout the body and prevent fluid leakage from blood vessels. The VAR was measured from the arm and leg using the finger and toe. Data was collected at the Fat Disorders Research Conference in Dallas Texas April 27-29, 2018 from 47 women with lipedema, and 7 controls, with additional participants enrolling. We used an iphone app called iPhysioMeter to measure pulse volume. The VAR was calculated as the means of pulse volume of the dependent limb (down) over the means of the pulse volume of the neutral limb (up). VAR was considered normal if it was less than one because pulse volume of a limb when it is down should be lower than when it is up. A VAR>1 was determined to be abnormal. The average VAR was normal in the hand among all the stages and controls. Among the feet the VAR increased as the stages increased. Stage 3 lipedema displayed abnormal average VAR in the feet (43% subjects had VAR>1), indicating that treatment of VAR may help reduce progression within and amongst stages.

Funding Source: Lipedema Foundation

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Burnett, Kiana; Herbst, Karen; Ussery, Christopher. "The relationship between lipedema and Venoarterial Reflex" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1631

Evaluating the Role of the KDELR in a Novel Form of ERAD

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Defects in protein quality control can lead to several diseases. To generate therapies, the various quality control pathways must first be identified. Quality control systems in the secretory pathway are essential for maintaining protein homeostasis, however these can be saturated when misfolded proteins accumulate in the endoplasmic reticulum (ER). Newly synthesized proteins that fail to acquire conformational maturation are selectively eliminated by endoplasmic reticulum associated degradation (ERAD). Although ERAD was traditionally thought to involve only clients retained in the ER, we have identified a stress-induced back-up checkpoint activation paradigm that operates in the Golgi complex. Null Hong Kong (NHK), a well-known ERAD substrate, binds to molecular chaperones that contain the C-terminal KDEL (Lys-Asp-Glu-Leu) motif. Protein clients that engage the novel recruitment system bind the KDEL Receptor (KDELR), which is also bound to Man1b1, a previously recognized ERAD component. The hypothesis to be tested is that the KDEL binding site plays an essential role to promote client recruitment by this novel system. If correct, then the site-directed mutation of this site in the KDELR is predicted to ablate co-immunoprecipitation and prevent NHK degradation. For this purpose, we generated KDELR169N, a ligand-binding-deficient mutant of the KDELR, and expressed it in 293T(WT) cells. Cell lysates will be collected, and western blot analyses will be performed. The findings that emerge from this experimental approach will provide the first mechanistic evidence as to whether the capacity of the KDELR-Man1b1 complex to accelerate NHK degradation relies on the binding of a KDEL signal by the KDELR.

Funding Source: NIH-NIGMS

Recommended Citation:
Diaz, Daniela ; Collette, John; Sifers, Richard. "Evaluating the Role of the KDELR in a Novel Form of ERAD" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1641

Derivatization of 3-Br-THC by Anionic Ortho-Fries Rearrangement

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Cannabis Sativa is a plant with rich therapeutic history and use in the treatment of pain, glaucoma, nausea depression, neuralgia, Multiple Sclerosis and HIV/AIDS symptoms. There are up to 750 natural products derived from Cannabis of which Δ^9- Tetrahydrocannabinol (Δ^9-THC) is the main psychotropic compound. Tetrahydrocannabinol Acid-A (THCA) is the biological precursor to Δ^9-THC and is relatively understudied. For analysis and distribution of THCA in food for instance, analytical standards are required to ensure quality distribution. Utilization of isotopically labelled derivatives represent a feasible solution. In this work we present efforts towards synthesizing isotopically labeled THCA. Westphal et. Al. (2017) has reported on Br-THC, an intermediary for synthesis involving late stage diversification via cross-coupling reactions. Herein, 3-Br-THC was elaborated to 2-Boc-3-Br-THC via Anionic Ortho-Fries Rearrangement.

Funding Source: NIH-NIGMS, ETH Z rich

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Small-molecule targeting of tau aggregation and propagation

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Tau aggregation underlies many neurodegenerative diseases collectively termed "tauopathies." Alzheimer Disease (AD) is the most prevalent tauopathy, and is characterized by progressive accumulation of tau aggregates in neurofibrillary tangles in the human brain. Recent evidence demonstrates that an important initial step in tau pathology is the transition of the tau monomer from a mostly inert, stable form to a seed-competent monomeric form. This seed competent monomer can then convert surrounding, inert tau monomers, leading to tau amyloid formation. These seed-competent aggregates are then able to transmit pathology through transcellular propagation in a prion-like manner, by interacting with cell-surfaceheparin sulfated proteoglycans (HSPG's) and subsequent cellular uptake. Considering these emergent aspects of tau pathophysiology, the principal aim of our investigation is to identify tau-binding small molecules thatstabilize the inert form of tau to suppress subsequent aggregation. After screening a 300,000 compound library we identified compounds that bind tau. We determined the binding affinities of a small number of lead compounds for tau using a surfacebio-layer interferometry (BLI) binding assay. Preliminary results indicate that several candidate compounds bind tau with micromolar affinity. Select compounds also blocked amyloid fibril formation, potentially through preferential stabilization of the inert conformation. These findings can be further extended to investigate whether the compounds that bind to tau will block tau uptake in vitro. Promising lead candidates will be developed as potential therapeutic agents.

Funding Source: NIH-NIGMS

C1QL1 synaptic protein mediates hyperacusis-like behavior

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The C1QL1 protein promotes synapse formation and/or maintenance in the central nervous system. However, in the peripheral nervous system, particularly the auditory system, the function of C1QL1 is unknown. Of the 2 types of sensory cells in the cochlea that detect sound, C1QL1 is unique to 'outer hair cells'. Hyperacusis is an exaggerated response to ordinary sounds in the environment, with varied reactions such as annoyance, fear, and/or pain. It affects approximately 1 in 50,000 people and can lead to difficulties in everyday life. We hypothesized that C1QL1 may play a role in the maintenance and/or formation of the outer hair cell synapses, which may modulate hearing (auditory sensitivity) or lead to auditory pain as the outer hair cell neurons resemble a somatosensory pain receptor. We first show that C1ql1 conditional knockout mice appear to hear normally. We then show that C1ql1 knockout mice appear to have an enhanced response compared to wildtype mice in the acoustic startle response assay. To ensure that these results are solely due to an auditory response, tactile startle response was performed as a control experiment. These results help support the hypothesis that C1QL1 may have a role in auditory pain and not in auditory sensitivity. Specifically, the lack of C1ql1 gene expression could contribute to hyperacusis. If our predictions are correct, we will have created the first successful mouse model to study hyperacusis.

Funding Source: NIH-NIGMS

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Corticosterone and hypothalamic gene expression in HPA-axis negative feedback activity and stress recovery time

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The hypothalamic-pituitary-adrenal (HPA) axis is an important endocrine pathway that regulates stress by releasing the hormone corticosterone (CORT). Differences are present in HPA axis activity between sexes. Females are shown to have a stronger HPA activation compared to males. We investigated the negative-feedback loop and sex differences in the HPA axis. To do this, gonadectomized and intact mice were restraint stressed for 20 minutes and were given a recovery time of either 0 min, 30 min, 60 min, 120 min. At this time, blood and brain samples were taken. A radioimmunoassay (RIA) was used to measure CORT in the blood and RT-qPCR was used to determine gene expression in the hypothalamus. RIA results for intact mice showed that females had higher amounts of CORT in the blood compared to males; CORT levels began to reach basal levels around the 120 mins regardless of sex. For the gonadectomized mice, females also had higher amounts of CORT in the blood and showed a longer recovery time compared to males. Males had greater expression of an early immediate gene, cFOS, compared to males at all time points, and in both sexes cFOS decreased as time progressed. In gonadectomized mice, the expression of cFOS over time was similar in both sexes. From these results, we can conclude that females had greater levels of CORT in the blood and less cFos expression compared to males. To continue this research, other parts of the brain known to be involved with stress response can be tested.

Funding Source: NIH-NIGMS

Recommended Citation:
Murillo, Josue; Mani, Shailaja. "Corticosterone and hypothalamic gene expression in HPA-axis negative feedback activity and stress recovery time" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1632

Neuromuscular Electrical Stimulation: A Pilot Study

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Obesity is a major issue contributing to a high prevalence of insulin resistance, cardiovascular disease, stroke, and type 2 diabetes. Despite the known benefits of exercise, physical activity levels remain low in the U.S. due to social and environmental barriers (lack of time/motivation, or inaccessible facilities). A third of the American population is considered overweight/obese, prompting the need for new methods to promote a healthier lifestyle. Neuromuscular electrical stimulation (NMES) utilizes electrical impulses to induce muscle contractions, commonly used in rehabilitation settings for injured muscle re-education. Prior studies have shown that skeletal muscle contractions (i.e., exercise) increase mitochondrial content (energy production) and glucose uptake (decreased insulin resistance) using both in vivo (exercise) and in vitro (electrical pulse stimulation of cultured human muscle cells) models. However, the effects of chronic NMES on energy metabolism and insulin sensitivity are unclear. The purpose of this study is to investigate the effects of 2 weeks of NMES on insulin sensitivity, metabolic function, and body composition. Six sedentary men and women completed 6 (20-minutes, 3x/week) sessions of NMES. Four surface electrodes were placed on the anterior aspect of the thigh muscle (two inches superior to the knee and two inches inferior to the inguinal region) with stimulation frequency set at 50Hz, 400μs, and an intensity tolerable by the participant. Insulin sensitivity, resting metabolic rate, anaerobic capacity, and body composition were assessed before and after the intervention. It is hypothesized that NMES will improve insulin sensitivity and metabolic function in sedentary adults.

Funding Source: NIH-NIGMS

Recommended Citation:
Orozco, Nicole; Jenkins, Jasmin; Galvan, Michelle; Bajpeyi, Sudip. "Neuromuscular Electrical Stimulation: A Pilot Study" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1659

Robotic Optimization of Surgical Procedure involved in Deep Brain Stimulation Studies

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In Deep Brain Stimulation (DBS) therapy, implanted electrodes are used to stimulate the basal ganglia of the brain to treat symptoms of Parkinson's Disease (PD) and other disorders. Despite its wide use, the mechanisms of DBS are not well-understood, and hence the best patterns of stimulation are not known. In this study, we are evaluating the effectiveness of a portable battery powered stimulator using a rat model of PD. To create Parkinsonian rats, animals are injected in one brain hemisphere with the dopamine-neuron-selective toxin, 6-OHDA (Tieu, K., 2011). In the same procedure, an array of electrodes is carefully inserted into the subthalamic nucleus (STN). By evaluating the efficacy of different intensities and patterns of stimulation using our battery-powered stimulator, we demonstrate its utility as a tool for optimizing DBS therapy.

The procedures for inducing the Parkinsonian state and placing DBS electrodes require precisely drilled craniotomies which are particularly difficult to perform and require a great deal of training. This allows our team to also engage in an engineering project in tangent with this DBS study. Using the methods proposed by (Ghanbari et. al., 2018) We have built a CNC microsurgical robot to perform craniotomies on the rodents used in our lab. By using an automated approach, the lab hopes that this system will reduce variability between studies.

Funding Source: Building Scholars

Recommended Citation:
Pacheco, Robert; Lewis, Erick; Kemere, Caleb. "Robotic Optimization of Surgical Procedure involved in Deep Brain Stimulation Studies" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1657

Correcting for Environmental Factors in Microbiome Wide Association Studies

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Research into the role that the microbiome plays in human health has helped identify microbes associated with diseases such as obesity and Crohn's disease. However, current microbiome studies do not account for variations in human anatomy, such as pH changes along the gut, which leads to many spurious associations. Furthermore, these variations increase the overall variance in the microbial abundance profiles, making it harder to distinguish between diseased and healthy microbiotas. To correct for these variations, we developed two new methods, "phylum normalization" and "reduced principal component analysis", and applied them to the largest pediatric Crohn's disease dataset containing more than 1,000 diseased and control samples. Each method tackled a different aspect of environmental noise in the data and was used in permutation tests to identify possible disease-causing taxa and for sample diagnosis classification. Phylum normalization, in which relative abundances are obtained by normalizing with respect to phylum taxonomic level counts, reduced the variance between samples—allowing for better classification of disease and control. Reduced principal component analysis, in which a specified number of components causing the greatest data variance are removed, decreased the number of disease-associated taxa, selecting 11 taxa compared to 55 without the method, while preserving classification power. Our methods could have applications in disease diagnosis and in prioritizing follow up studies on potential pathogens. Future work would entail validating results with different datasets and other feature selection methods.

Funding Source: NSF REU, NIH-NIGMS

Recommended Citation:
Patino Calero, Michelle; Birzu, Gabriel; Korolev, Kirill. "Correcting for Environmental Factors in Microbiome Wide Association Studies" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1684

Acute dietary nitrate supplementation has no significant effect on wasted left ventricular energy in young healthy individuals.

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Cardiovascular disease is the leading cause of death worldwide and is associated with low levels of Nitric Oxide (NO) bioavailability. NO is a vascular protective agent which could increase through dietary nitrate supplementation. Wasted left ventricular energy (LVEw) represents the added workload the ventricle produces during the reflecting pressure wave within a cardiac cycle. It is wasted because there is no blood flow gain produced. LVEw is associated with arterial stiffness and refractory angina syndrome. Higher levels of NO are associated with lower cardiovascular risks. Therefore, increased NO through dietary nitrates might reduce LVEw. The purpose of this study is to determine the response of an acute dietary nitrate supplement in LVEw via noninvasive pulse wave analysis (PWA). A double-blind, cross-over study was performed in 17 young, healthy subjects (18 to 24 years old). Four lab visits were scheduled within 10 days; first 2 visits back to back and the last 2 visits one week after. Subjects followed a low-nitrate diet for 3 days; two days prior to the first and third lab visits. Two hours before visits 2 and 4, subjects were asked to drink 800 mg of nitrate or placebo. LVEw was calculated: =((π/4) x (Ps-Pi) x (ED - ΔTp) x 1.333) via PWA. A two-way repeated measurements ANOVA was performed with significance set at alpha=0.05. LVEw ranged from 736 ± 644 dyne•s•cm-2 at baseline in males to 997 ± 917 dyne•s•cm-2 after placebo, also in males and there was no significant interaction. These results show that an acute dose of dietary nitrate supplement has no effect on LVEw in young healthy individuals.

Funding Source: NIH-NIGMS, Building Scholars

Recommended Citation:
Rascon, Jozelyn ; Morales, Francisco; Gurovich, Alvaro. "Acute dietary nitrate supplementation has no significant effect on wasted left ventricular energy in young healthy individuals." (2018). COURI Symposium Abstracts, Fall 2018, ID= 1627

In vitro evaluation of metformin hydrochloride dose-response on transdermal, nasal, and buccal human cell lines

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Cell viability plays a major role in pharmaceutical studies considering the most effective drug delivery system in efforts to achieve desired dose response. Metformin hydrochloride (HCl) is an oral antidiabetic drug widely used in the United States to treat type 2 diabetes mellitus. This study evaluates cell viability and dose-response of metformin HCl on transdermal, nasal and buccal mammalian cell lines. Metformin HCl is characterized as having a low systemic bioavailability due to being challenged by the drugs' high-water solubility and its variable intestinal absorption. The aim of this study was to provide an in vitro evaluation to ultimately determine if the given cell lines may be proven effective in the absorption of metformin HCl. Cell images were taken to reveal the morphology of each cell line before conducting a cell viability assessment utilizing a resazurin assay. In addition, Air-Liquid Interface Culture Condition (ALI) and Liquid Covered Culture Condition (LCC) systems were performed to mimic human epithelial cellular absorption in RPMI 2650 nasal epithelium cell line. ALI and LCC conditions were compared to determine if conditions resulted more significantly reliable in determining cell viability in RPMI 2650 cell line. Among the cell lines reviewed in this study, all resulted promising with viability values ranging from 87.76% to 144.36% within the drug concentrations delivered into each cell line. Consequently, the transdermal, nasal, and buccal cell lines resulting in high cell viability and effective dose-response treated with metformin HCl, may allow for future developmental formulation studies to treat hyperinsulinemia derived cancers.

Funding Source: NIH-NIGMS

Towards the identification of reproducible and reliable outcome measures for preclinical trials in a mouse model of Tuberous Sclerosis

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Monogenic neurodevelopmental disorders (NDDs) represent a fraction of the neurological disease burden upon society. Research focused on NDDs has helped further our understanding of the pathophysiology of autism spectrum disorder(ASD). An example is Tuberous Sclerosis(TS), an autosomal dominant disorder caused by mutations in TSC1 or TSC2. Cognition and social behavior deficits are prevalent in this disorder, and animal models have been used in attempts to study TS. However, issues of reproducibility are a growing concern in animal model studies in the field of brain disorders. Therefore, we performed a study of Tsc mouse models to better understand the extent phenotypic outcomes reported in literature are reproducible. Tsc2+/- and wildtype littermate mice(N=60, N=14-16 per sex and genotype) were evaluated for anxiety-like behavior, locomotor function and spatial memory in an elevated plus maze(EPM), open field assay(OFA), light/dark(LD), and Morris Water Maze test(MWM). Tsc2+/- mice were projected to display normal levels of anxiety-like behavior and locomotor activity but diminished spatial learning and memory in MWM. Results demonstrated no significant differences in anxiety-related behaviors and exploratory behavior in EPM and OFA ($p > 0.05$; two-way ANOVA) but increased anxiety-like behavior in LD in Tsc2+/- males. In MWM, genotype did not affect learning ($p > 0.05$; linear regression). In a probe for short-term and long-term memory, Tsc2+/- mice failed to demonstrate diminished memory($p > 0.05$; two-way ANOVA). The lack of anxiety and exploratory behavior phenotypes were supported by previous reports while the absence of a learning and memory deficit is discordant. Before studying novel interventions, it may be of interest to pursue alternate animal models.

Funding Source: NIH-NIGMS

Recommended Citation:
Torres, Dina; Soriano, Sirena; Samaco, Rodney. "Towards the identification of reproducible and reliable outcome measures for preclinical trials in a mouse model of Tuberous Sclerosis" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1701

Mechanism of Pathogenesis of Proliferative Vitreoretinopathy

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Proliferative vitreoretinopathy(PVR) is characterized by migration and proliferation of retinal-pigmented epithelial cells (RPE) into the vitreous caused by ocular trauma and/or retinal breaks leading to visual loss. PVR is the greatest obstacle in retinal reattachment surgery, being the cause of 75% of unsuccessful surgeries. Patients with PVR have elevated interleukin 6(IL-6) levels in the vitreous, however, its role in PVR is unclear. IL-6 has two modes of action: through "classic-signaling" pathway by binding the membrane IL-6 receptor α(mIL-6R) which is anti-inflammatory, and "trans-signaling" pathway through the soluble IL-6 receptor(sIL-6R) which is pro-inflammatory. The IL-6/IL-6R complex engages with membrane glycoprotein 130(gp130). Soluble gp130 inhibits IL-6 trans-signaling pathway, which slows progression of chronic inflammatory processes. Our hypothesis is that IL-6 trans-signaling contributes to PVR. Our goal is to develop a mouse model of PVR by injecting dispase in the vitreous, which causes inflammation, proliferation, and migration of RPE cells. Then using recombinant sgp130Fc to inhibit IL-6 trans-signaling, we will assess whether it can prevent PVR. We injected 3µL of dispase and PBS in the contralateral eye. For 2 weeks, we performed ophthalmoscopic examinations. Our results shows only the eyes injected with dispase developed PVR. Our next step is to inject sgp130Fc/dispase in one eye and PBS/dispase in the other. After 3 weeks, we will harvest the eyes for examination and immunohistochemistry detection of the proliferation marker Ki67. We expect that our results will fill the gap-in-our understanding of PVR pathogenesis and allow us to develop novel therapy for the disease.

Funding Source: NIH-NIGMS

Recommended Citation:
Wilson, Alexis; Tosi, Joaquin; Howard, Tamara; Gonzalez-Bosc, Laura. "Mechanism of Pathogenesis of Proliferative Vitreoretinopathy" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1662

Environmental Health 2

Screening for Wolbachia in Arthropods from different locations in El Paso, TX

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Wolbachia is an endo-parasitic bacterium capable of establishing symbiotic relationships with numerous species of arthropods. Research on Wolbachia has expanded over the recent years as scientists strive to gain a better understanding of Wolbachia's complex relationship with its hosts. Wolbachia causes changes to its host by feminization, cyptoplasmic incompatibility, and Parthenogenesis. Wolbachia does not infect humans but shows promise in reducing the spread of viral diseases that are spread by mosquitoes . Previous studies at El Paso Community College have found insects in El Paso infected with Wolbachia. The focus of this study is to screen insects collected in the El Paso region for infection with Wolbachia by using PCR to amplify a portion of the 16s Ribosomal DNA specific to Wolbachia. Insects were collected in the North East area of El Paso and identified down to the order level. DNA was then extracted from the collected insects. Following the PCR step, DNA gel electrophoresis was used to look for the presence of a band of approximately 438 bp, the expected size of the PCR product. Insects that were tested include ants, beetles, mosquitos, cockroaches, wasps, larva, and crickets. None of the insects were positive for Wolbachia except for the same species of mosquitoes. Five positive results were obtained with all coming from collected Culex quinquefasciatus mosquitos. DNA sequencing will be performed in the future to confirm Wolbachia infection in the five Culex quinquefasciatus and to determine which strain of Wolbachia is infecting them.

Recommended Citation:
Dichristina, Italia; Torres, Sebastian; Marquez, Angelica; Chianelli, Xiomara. "Screening for Wolbachia in Arthropods from different locations in El Paso, TX" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1703

Determining the possible fecal contamination of soils impacted by flood water during Hurricane Harvey

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In August 2017, Hurricane Harvey dropped an unprecedented 30 inches of rain in the Houston Metropolitan Area submerging 25% of Harris County in flood waters and displacing 30,000 residents. During flood events, sewage systems can become compromised releasing raw sewage and exposing the impacted area to fecal pollution. The use of previously flooded outdoor areas is a concern due to the potential of microbial contamination (bacterial and viral). Bacterial source tracking (BST) is used to test for the presence of potential pathogens. The objective of this project is to estimate fecal contamination in soils impacted by the flood water. Fecal pollution and the potential presence of enteric pathogens is typically determined by measuring the presence of fecal indicator bacteria such as *E. coli* and *Bacteroidales*. Fecal indicator bacteria occur at high levels in fecal pollution sources, and testing is easy and inexpensive. For this project, quantitative polymerase chain reaction (qPCR) library-independent BST methods were used to identify human and animal sources of fecal pollution impacting flooded communities. Forty soil samples were collected from residential areas impacted by Hurricane Harvey approximately 2 weeks after the flood events. Bacterial DNA was extracted from soil samples and analyzed using real-time qPCR for the *Bacteroidales* GenBac3 general, HF183/BacR287 human, CF128 ruminant, and Helicobacter GFD bird qPCR markers. Quantifying these markers in soil sample DNA extracts provided estimates of possible fecal impacts. A high frequency of detection suggests there is a high probability of presence of enteric pathogens in the soil and possible exposure risk.

Funding Source: NIH-NIGMS, BUILDing Scholars

Recommended Citation:
Lerma, Melissa; Truesdale, Joy; Rodriguez, Roberto. "Determining the possible fecal contamination of soils impacted by flood water during Hurricane Harvey" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1629

Isolating Antibiotic Resistant Bacteria from Faucets and Sinks

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Nosocomial infections have become a significant problem in clinical settings. Recently, several bacteria have been linked to water sources that travel to the patient either in aerosols or directly by patient contact from their provider. Sink faucets where providers wash their hands are equipped with aerators that provide an environment where bacteria can form bio-films, which can then spread bacteria. To compound the problem, some of the bacteria may be resistant to multiple antibiotics. The objective of this study is to isolate and identify bacteria in biofilms from faucet components, sinks and water samples, and to determine their antibiotic resistance. Five samples were collected from clinical settings and four samples were collected from schools for this study. The MicroScan autoSCAN 4 Bacterial identification system was used to identify the bacterial isolates and to determine the antibiotics which these organisms are resistant to. Our results showed the isolation of various species of Gram negative bacteria such as Vibrio spp. And Gram positive bacteria including S. scuri, S. hominis-homin, and S. auricularis which have been linked to nosocomial infections. Out of fifteen isolates; thirteen isolates were identified with a probability of correct identification of 84.55 % or above. Out of 3 Vibrio isolates, 2 were resistant to more than 2 antibiotics. Out of 9 Staphylococcus isolates, 3 were resistant to more than 2 antibiotics. Our results show that sinks and faucets are capable of harboring bacteria that can potentially cause nosocomial infections, especially in debilitated or immunocompromised patients.

Recommended Citation:
Lopez, Arely; Maldonado, Elizabeth; Marquez, Angelica; Mendoza, Jose; Alvarez, Maria. "Isolating Antibiotic Resistant Bacteria from Faucets and Sinks" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1707

Isolating Antibiotic Resistant Bacteria from the Rio Grande River

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The Rio Grande River is an important water resource for the U.S.-Mexico border region. Microbial Pollution from rain runoff, municipal streams, and direct animal and human contact has been documented frequently along this river segment. Since the emergence of multi-drug resistant bacteria is currently as world-wide crisis, the identification of potentially pathogenic bacteria with high resistance to antibiotics is of paramount importance in our international border region. The objective of this study is to determine if bacteria from the river exhibit high resistance to antibiotics commonly used in the clinical setting. We hypothesize that potentially pathogenic bacteria showing resistance to multiple antibiotics will be isolated from the river. Water samples were collected from three Rio Grande River sites close to the Texas New Mexico State line. Standard membrane filtration techniques were used to isolated bacteria. Filters were placed on media selective for Gram negative or Gram positive bacteria including MUG, MacConkey, M-Endo and MSA. Select colonies were transferred to Tryptic Soy Agar (TSA) and incubated for 24h at 37^{o}C. Forty six isolates were gram stained and analyzed by the MicroscanAutoscan4 bacterial identification system using panels for the identification of gram negative and gram positive bacteria. Thirty nine isolates were identified with a probability of correct identification of 82.16% or higher. Out of 27 Gram negative isolates, five potentially pathogenic bacteria including Vibrio spp., Klebsiella pneumoniae, Ewingella, Aeromonas and Sphingomonas were resistant to at least two individual antibiotics. Vibrio cholera, E.coli and Ewingella were resistant to at least one synergistic combination of antibiotics. Out of 12 Gram positive isolates, 10 (83%) belonged to the genus Staphylococcus and included potentially pathogenic species including aureus, sciuri, auricularis, hemolyticus, schleiferi and xylosus. Eight of the Staphylococcus isolates were resistant to at least two individual antibiotics and four were resistant to at least one synergistic combination. Our results show the presence of potentially pathogenic Gram positive and Gram negative bacteria with resistance to multiple antibiotics in the Rio Grande River. The presence of bacteria already resistant to multiple antibiotics and the ability of bacteria to transfer genetic elements that confer antibiotic resistance is an area of great concern for our international community.

Recommended Citation:
Wilkerson, Delina; Rojas, Nicholas; Mendoza, Jose; Alvarez, Maria. "Isolating Antibiotic Resistant Bacteria from the Rio Grande River" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1704

Health Disparities 2

Assessment of Sensory Function in Individuals Experiencing Homelessness

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Sensory function is the body's process which allows individuals to navigate through their daily life. Based on prior studies, individuals experiencing homelessness are at increased risk for poor sensory function. Poor sensory function has been hypothesized to be associated with daily competence and functional independence. The specific aim of this research project was to assess sensory function in individuals experiencing homelessness and its relationship to functional independence. Approximately, 50 individuals from shelters across the City of El Paso were assessed for sensory functions (visual, auditory, gustatory, olfactory, and tactile), sensory integration, and functional independence using a standard Snellen Chart, Etymotic Research Hearing Test, identification of four taste strips, Sniffin' Sticks Screening 12-Test, 2-point discrimination test, Quick Neurological Screening Test-3rd Edition Revised, and a self-rated questionnaire, respectively. Participants completed an interview regarding sensory deficits, challenges related to them, and requirements of a solution as part of the inspiration phase of the Human-Centered Design (HCD) process. Preliminary results indicated sensory deficits related to visual acuity and hearing are prevalent within the homeless population and may provide additional challenges for the chronically homeless. Preliminary analysis of interviews has provided insight into the challenges encountered when attempting to successfully exit homelessness, including challenges in performing activities of daily living. Assessing sensory function in individuals experiencing homelessness is important because sensory deficits may negatively impact an individual's abilities, independence, and quality of life. The data collected will be used to direct the development of an intervention aimed to improve sensory function using an HCD approach.

Funding Source: NIH-NIGMS

Recommended Citation:
Alvarado, Daisy; Kendall, PhD, Meagan. "Assessment of Sensory Function in Individuals Experiencing Homelessness" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1668

Doctor, Doctor, Give me the News: Patient Satisfaction in the Infertility Diagnostic Process

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The literature on patient satisfaction varies widely, yet there is less in regards to the difference between generalists and specialists, and no literature on the difference between generalists (e.g. Obstetricians/ Gynecologists) and specialists (e.g. Reproductive Endocrinologists) regarding patient satisfaction with infertility diagnosis and treatment. Providing insight into patient views of the diagnostic and treatment process is helpful for future fertility patients who will be experiencing life-changing challenges, and for health professionals who strive to ensure better patient satisfaction. Interview data from 20 women and 8 men who underwent fertility treatment between 2002 and 2008 are utilized in this research. Our data reveal that both generalists and specialists dismissed respondent's personal knowledge and individual differences concerning their own bodies. Differences emerged in how generalists tended to view the female body as more "normal" and thus easily able to become pregnant. Thus, generalists did not pursue diagnostic testing as quickly as specialists. As women became frustrated, they sought further diagnostics from specialists. Thus, for these patients, satisfaction was evaluated in terms of the care and services that were provided to them by generalists and specialists. This raises questions such as whether providing patients with more personalized care, engaging in active listening, and providing sufficient knowledge on fertility treatments helps improve overall satisfaction regardless of the outcome (i.e. pregnancy).

Funding Source: NIH-NIGMS

Recommended Citation:
Bombach, Brianne; Leyser-Whalen, Ophra. "Doctor, Doctor, Give me the News: Patient Satisfaction in the Infertility Diagnostic Process" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1638

Understanding the Emotional Well-being of Prosthetic Limb Recipients in Mexico

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Lower limb amputees in developing countries often experience issues with mobility that may lead to a loss of economic sustainability, social circles, and independence. Due to these circumstances, the loss of a limb makes adjusting to life difficult by creating unwanted burdens. The impact of receiving a prosthesis helps restore mobility and also aids in transforming peoples' lives one step at a time. However, there are issues that are often overlooked in the healing process. The purpose of this study is to understand the emotional well-being of prosthetic limb recipients. Through a mixed-methods approach, the present study investigates the lived experiences of prosthetic limb recipients in four sites throughout Mexico (Oaxaca, Guadalajara, Mexico City, and Cuernavaca). Ethno-surveys and in-depth, face-to-face interviews were conducted in Spanish with prosthetic limb recipients, family members, and physical therapists. Data shows that more than 60% of prosthetic limb recipients have not felt an impact on their emotional well-being during the past two weeks. The in-depth interviews supports this data. Results will provide a better understanding of how emotional well-being is affected due to living with a prosthesis.

Funding Source: NIH-NIGMS

The Impact of Progressive Marijuana Policy on Number of Arrest of Racial and Ethnic Minorities

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The extant literature has shown that conservative policies on the criminalization of marijuana have historically been used as a tool to target and stigmatize people of color. The criminalization of marijuana has contributed to the disproportionate mass incarceration rate of people of color in the prison industrial complex. To counteract failed drug war policies, eight states thus far have legalized and/or have decriminalization the drug. However, few studies explore whether existing policy platforms still result in the marginalization of people of color even after legalization. Therefore, this study examines the role of racial and ethnic populations and progressivity of marijuana policy on number of arrests for possession. Our argument is twofold: 1) more progressive marijuana policies enforcing the decriminalization of marijuana greatly decrease the number of arrests and detentions due to possession over time, and 2) the effect of existing policies, regardless of progressivity, differ by race and ethnicity. To test this relationship, we make use of NORML data and the American Community Survey to employ a content analysis of marijuana policies and arrest numbers across states before and after legalization. The findings suggest that progressive policies, such as expunging criminal records and protection against employment discrimination, will aid minorities in benefitting socioeconomically from the legalization boom.

Funding Source: NIH-NIGMS

Recommended Citation:
Fuentes, Ana; Sanchez , Gabriel. "The Impact of Progressive Marijuana Policy on Number of Arrest of Racial and Ethnic Minorities" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1661

One-Year Snapshot of National Labor Trafficking

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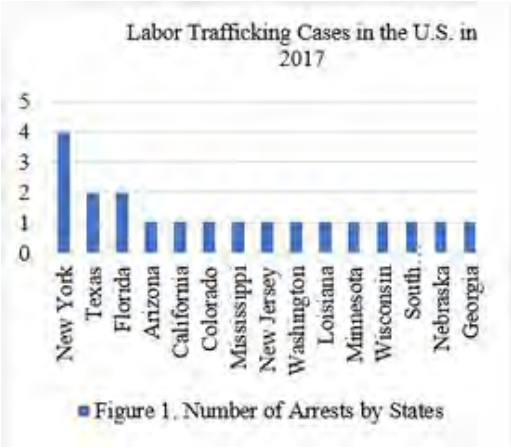
Due to its hidden nature of crimes, it is very difficult to estimate the global-scale of labor trafficking. Over the past decade, the Federal Bureau of Investigations (2016) has reported that they have assisted in the arrest of more than 2,000 human traffickers of both sex and labor trafficking, but labor trafficker-focused research primarily has relied on small convenience samples with limited ability to compare across time.This study uses a systematic search method to determine the incidence of arrests for labor trafficking in the U.S. in 2017. The findings from this report include individual and case details including characteristics of the labor traffickers (gender, race, age, method of violence), details about how they recruited and victimized their forced labor victims, and information about their case resolutions. Out of 50 states in the U.S., there are 15 states that have arrest cases for labor trafficking. 45% (n=9) of the cases involved a trafficker in more than one person. 88.9% (n=16) of the traffickers were male, and only 11.1% (n=2) of the traffickers were females. Interpretation of this study should be done with caution, as with all cross-sectional studies. The primary limitation of this study is lack of data. The research team used a structured and systematic strategy to capture all of the labor trafficking of migrant laborer and U.S. national cases in the U.S. that resulted in the arrest of a labor trafficker; however, some cases may not have been reported by the media or by law enforcement and prosecutors.



Funding Source: NIH-NIGMS

Recommended Citation:
Macias, Sofia; Lul, Bandak; Roe-Sepowitz, Dominique. "One-Year Snapshot of National Labor Trafficking" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1624

An investigation of Latino health outcomes: Implications of the Affordable Care Act

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The Affordable Care Act (ACA) was implemented to combat disparities in health care access and utilization, yet few studies have tracked its implications on racial and ethnic minorities. Previous literature indicates that the Latino population experiences higher rates of many chronic physical and mental health problems. Latinos also demonstrate a longstanding history of disparities in access to care, utilization of care and insurance rates. Thus, this study aims to investigate multiple implications of the ACA provisions on the Latino population. Our hypothesis predicts that measures of health care access and utilization, insurance rates, self-rated health and other health-related outcomes will differ significantly between years before the ACA was implemented and years after said provisions. Using the National Health Interview Survey, the present study utilizes data from years prior to (2010-2013) and after the ACA's provisions were implemented (2014-2016) to investigate said relationships. This project further aims to fill gaps in the literature by including questions related to mental health care use and behaviors. To examine the relationship between the implementations of the ACA and various Latino health outcomes, we employ a series of descriptive and bi-variate statistics (Chi-squared and t-tests) to build ordinary least squares (OLS) and logistic regression models. Analyses are currently underway. However, preliminary results of this study imply that the Affordable Care Act has had a meaningful impact on the Latino population and that any future reforms to health care should consider the role of these findings.

Funding Source: NIH-NIGMS

Recommended Citation:
Najera, Sarah ; Cartwright, Kate. "An investigation of Latino health outcomes: Implications of the Affordable Care Act" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1644

Re-integration into communities and everyday society for prosthetic limb recipients in Mexico

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Mexico has a large population of amputees that are in need of prosthetic limbs. According to LIMBS International, a non-profit organization that provides low-cost, affordable prosthetic limbs to people across the world, "It is estimated that there are over 3 million amputees throughout Mexico" (http://www.limbsinternational.org/mexico.html). One of the issues that remains of concern is the (re)-integration of prosthetic limb recipients into their communities and everyday society. In order to better understand how prosthetic limb recipients integrate into Mexico's society a mixed-methods approach involving an ethno-survey and in-depth, face-to-face interviews in four sites across Mexico (Oaxaca, Guadalajara, Mexico City, and Cuernavaca) was conducted during summer 2018. Studying the quality-of-life for an amputee in a developing-country will give researchers a better understanding of the ways in which prosthetic limb recipients live their lives and how they navigate their social world. This helps inform the ways in which healthcare service providers may assist limb recipients during the rehabilitation process. Findings suggest that prosthetic limb recipients feel as though they are re-integrating into their social environments. There is still a large population not receiving the rehabilitation services that could help them re-integrate into society, which could be looked at and compared to for future research.

Funding Source: NIH-NIGMS, LIMBS International

Recommended Citation:
Williams, Rachel; Cordero, Katerina; Armendariz, Sergio; Renteria, Roger; Murga, Aurelia. "Re-integration into communities and everyday society for prosthetic limb recipients in Mexico" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1699

Infectious Diseases 2

Expression and Purification of SUMO Activating Enzyme 1 and 2 (SAE1/SAE2) for Viral Protein Interaction Studies

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SUMOylation is a post-transcriptional modification system that is essential to numerous cellular functions including DNA repair, cellular response to stress, and transcriptional regulation through the cell cycle. In recent studies, disruptions in the SUMOylation pathway have been shown to have a role in health ailments such as cancer and neurodegenerative disease. SUMO activating enzyme 1 and SUMO activating enzyme 2 (SAE1/SAE2) facilitate the binding of small ubiquitin-like modifier (SUMO) proteins to target proteins, which leads to the modification of their functions. SAE1/SAE2 activity is obstructed by the avian adenoviral protein, GAM1, resulting in the global inhibition of cellular SUMOylation. This study aims to determine the complex structure of the GAM1 and SAE1/SAE2, which would provide useful insight of their interaction and GAM1's role of SUMOylation regulation. For this study, SAE1 and SAE2 were cloned as a single peptide with flexible linker between them in previous studies. The conjugated construct was obtained and transformed into E. coli BL21 competent cells. Protein expression protocols were optimized to increase yield and solubility of both the recombinant proteins. Soluble protein was purified using affinity chromatography. A high yield of soluble pure complex will be used for functional and structural studies with purified GAM1 protein that will enhance our understanding of the mechanism behind virus-host protein-protein interaction and possibly revealing a target for anti-viral therapies.

Funding Source: NIH-NIGMS

Detecting Mycobacterium avium paratuberculosis as the presumed infectious cause of Crohn's disease

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Crohn's disease (CD) is a chronic inflammatory bowel disease (IBD) of unknown cause. Because of its similarities to Johne's disease, a chronic enteritis of ruminant animals caused by M. avium paratuberculosis (MAP), it has been considered that MAP could be the etiological agent of CD. More studies are needed to confirm a link between detecting MAP in CD patients and a role in causation. We hypothesized that MAP can be detected in peripheral blood cells of CD patients more frequently than in non-IBD controls, and multiple blood samples are required to confirm MAP infection. To test this, consenting CD patients from Baylor College of Medicine Clinic and non-IBD controls provided whole blood samples. Samples were separated into PBMCs followed by DNA extraction and testing to detect the MAP IS900 gene by PCR. DNA was extracted from a total of n = 98 peripheral blood samples and tested the DNA by nested PCR. MAP IS900 detection was not confirmed in any DNA sample tested. Samples were re-tested with equivocal results using real time PCR which resulted in no MAP detection. However, in parallel studies, acid fast staining for mycobacteria spp. showed positive results in some patient blood samples, suggesting there may be technical limitations in DNA detection. Therefore, we worked to optimize a protocol to detect MAP proteins in human blood samples by Western blotting using Mab 17A12. These results show that improved detection of MAP in human samples will be required to reliably test whether CD is associated with MAP infection.

Funding Source: NIH-NIGMS

Recommended Citation:
Moreno, Diana; McNees, Adrienne; Graham, David. "Detecting Mycobacterium avium paratuberculosis as the presumed infectious cause of Crohn's disease" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1650

Attitudes and Immunization

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Although the efficacy and safety of immunizations have been validated in numerous studies, immunizations still face controversy and resistance. In particular, the Measles, Mumps, and Rubella (MMR) and Human Papilloma Virus (HPV) vaccines have proven to be especially controversial. However, little research has been done to see which factors predict the likelihood of parents vaccinating their children. In order to assess which factor is most predictive of parental intentions to vaccinate for MMR and HPV, we used the Theory of Planned Behavior (TPB), which states that there are three factors that contribute to whether or not a person will intend to perform a behavior. We wanted to see which aspect of TPB is most predictive of intention to immunize and to see if this was affected by cultural self-construal. We predict that subjective norms would be most predictive of immunization intentions for participants with an interdependent self-construal, whereas attitudes would be more predictive of intentions for participants with an independent self-construal. Hierarchal multiple regressions were run in order to determine which factor is most predictive. We determined that for the MMR vaccine, attitudes were the biggest predictor of immunization intentions, while for the HPV vaccine subjective norms were the biggest predictor of immunization intentions. The only observed interaction with self-construal was for HPV attitudes. No other interactions between self-construal and attitudes or subjective norms were found.

Funding Source: NIH-NIGMS

An unexpected finding leads to a new project: Exploring how Leishmania spreads from cell to cell

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Leishmaniasis is a neglected tropical disease caused by the Leishmania parasite. Each year, approximately 2 million people experience disfiguring cutaneous ulcers or visceral disease. Current drug treatments are few and the concern for developing antimicrobial resistance along with associated cardiac, renal, and hepatic toxicity calls for novel therapies for leishmaniasis. Leishmania must live inside macrophages to survive in people and cause disease. The Wetzel laboratory has found that drugs that block parasite uptake by macrophages, such as the kinase inhibitors imatinib and bosutinib, decrease the manifestations of leishmaniasis in mouse models. One of the key goals in our laboratory is to improve the efficacy of these uptake inhibitors. Typically, parasite uptake by macrophages is quantified with immunofluorescence-based high content-imaging systems. To validate an alternate quantification method, we generated transgenic L. amazonensis parasites (L. amazonensis^{luc}) that stably express the Luciferase reporter gene. We then exposed Bone Marrow-Derived Macrophages (BMDM) to increasing concentrations of drug (imatinib, bosutinib or the standard antileishmanial drug miltefosine), infected them with L. amazonensis^{luc} amastigotes or promastigotes, and measured the luciferase signal from both external and internal parasites. The uptake EC_{50}'s (Effective concentration that inhibits 50% of parasite uptake by macrophages) estimated here are in accordance with our previous data, thus validating the luciferase reporter assay as an alternative method for quantifying parasite internalization. We will next use this method to determine whether combining kinase inhibitors with standard drugs for leishmaniasis improves their efficacy while limiting their toxicity.

Funding Source: NIH-NIGMS, DMW is supported by K08108031, a CCRAC Earl

Recommended Citation:
Piña, Alejandra; Ullah, Imran; Wetzel, Dawn. "An unexpected finding leads to a new project: Exploring how Leishmania spreads from cell to cell" (2018). COURI Symposium Abstracts, Fall 2018, ID= 1653

Translational Biomedicine 2

Hydraulic integration and optimization for the M3 Knee

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The M3 mechanical knee is a low-cost, four-bar above knee prothesis that has been developed by LIMBS International. Previous work was done to redesign the knee for an electronic, microprocessor-controlled application that is both, effective and low-cost. Additionally, an analysis of the kinematics of the knee was used to determine the best attachment point for an actuator. Hydraulics were chosen because of their versatility as well as high power output. One of the benefits hydraulics offers over other systems, such as pneumatics, is the durability and lack of complexity when being repaired or maintained. Based off the previous redesign of the M3 knee, the implementations of hydraulic systems require a series of specifications that must to be met by the components. The determination of these specifications were obtained from the kinematic analysis of the knee. The weight limitation is 0.75 kg and the volume limitation is 130 cm^3. The gait cycle, taking normally 1.2 seconds, was used to determine the velocity. The velocity of the piston is 4.16 cm/s during the maximum stroke of 2 cm. Although the stroke and velocity are constant for all the components, the rest of the specifications are dependent on the physical characteristics of the whole system. The results are expected to optimize the current hydraulic system design by researching components that could improve the use of space and performance, as well as maintaining a low cost overall.

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Superparamagnetic Fe3O4 Magnetic Nanoparticles: Examination of their Feasibility for Hyperthermia Treatment for Cancer

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Magnetic Iron Oxide nanoparticles (IONPs), specifically Fe_3O_4, have attracted the attention of scientists for medical applications due to their biocompatibility, low cost, and drug delivery capabilities, they can carry anticancer drugs to a desired location within the human body. Subjecting IONPs to an alternating current(AC) magnetic field the IONPs will convert energy stored into heat exposing the cancerous tumors to intolerable conditions. The focus was the structure and magnetic moment of our IONPs through multiple simulations in various types of equipment. The temperature of the heat generated when exposed through an AC magnetic field is critical to the success of our hyperthermia treatment. The specific absorption rate (SAR) of the particles influences how the body will react to insertion of the IONPs. For this review we used three samples of IONPs, BM002, BM003, and BM004. With the help of a vibrating sample magnetometer (VSM) the magnetic moment at room temperature, measured in emu/g, was able to be observed and documented. BM002 had the highest measurement of magnetization at 108.34 emu/g. While BM004 had the lowest measurement at 73.99 emu/g. When measuring the particles with X-ray Diffraction (XRD) the results offered a crystallite size of 43-65 nm in diameter for our three samples. In addition to XRD, we were able to use a scanning electron microscope(SEM) to identify the exact size and shape of our particles. All 3 samples contained particles within a range of 63-128nm in diameter displaying a spherical-like shape. Through the hyperthermia machine, the results yielded a specific temperature of the IONPs when exposed to an electromagnetic field composed of radio frequencies. Our results, see figure 1, showed that the specific absorption rate for our three samples were from 0-160 W/g. In conclusion, we have determined through our results that our particles can be used for different medical applications including drug delivery and hyperthermia therapy treatment for cancer.

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Gadolinium-Based Contrast Agent-Induced Adverse Events: An assessment of contributing factors

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Background. Gadolinium, a toxic rare earth element, is ideal for enhancing magnetic resonance images. Proprietary polyamine chelates binding gadolinium have been formulated to take advantage of its paramagnetic properties while reducing the metal's toxicity. Although gadolinium-based contrast agent-associated adverse events are rare, the threat of litigation has vastly altered clinical practice.

Methods. Patients with and without exposure to gadolinium-based contrast agents were matched and compared using the Truven Health MarketScan Databases; these are epidemiologic databases that provide large sample of unique, integrated patient-level data. STATA was used for quantitative analysis.

Results.The Food & Drug Administration recently held a meeting to address concerns about gadolinium-based contrast in patients—regardless of renal function. Factors such as age, sex, existing health conditions, and type of health coverage were examined.

Conclusions. This study provides a more comprehensive guide to medical professionals for the use of gadolinium-based contrast, and subsequent evaluation and diagnosis of its adverse effects.

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The role of Drosophila Snazarus in the regulation of fat body lipid droplet morphology and organization

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Lipid Droplets (LDs) are cytoplasmic organelles rich in triacylglycerides (TAG) and sterol esters, which serve as primary energy stores that can be mobilized during prolonged fasting. How cells functionally organize fat stores for efficient mobilization during nutrient stress remains poorly understood. The purpose of this study was to investigate how Drosophila fat body adipocytes functionally and spatially organize LDs, and identify a novel role for sorting nexin protein Snazarus (Snz) as a regulator of LD homeostasis. We find that Snz localizes to peripheral LD-Plasma Membrane (pLD-PM) contact sites and regulates pLD homeostasis. Loss of Snz alters PM architecture and perturbs pLD whereas over-expressing Snz increases pLD size and TAG production. Snz functionally interacts with fatty acid processing enzyme Desat1, indicating a role in nutrient flux at pLD-PM contact sites. Disruptions in LD biogenesis or pathological lipid accumulation obstruct normal cellular functions which lead to metabolic diseases such as obesity and type 2 diabetes. Therefore, understanding the mechanisms responsible for cellular LD dynamics will potentially have a substantial impact on human health and the treatment of metabolic diseases.

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Standardization of a Dot Blot Protocol to Assess Changes in Total Cellular SUMO-1 Upon Stress

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Small ubiquitin-like modifiers (SUMOs) are conjugated to target proteins through the formation of an isopeptide bond between the C-terminus of SUMO and a lysine residue in the target, a process known as SUMOylation. SUMOylation regulates protein function by affecting protein cellular localization, activity, stability, and interactions with other macromolecules. SUMOylation is affected by chemical inhibitors and cellular stress. This study aims to standardize a method to accurately quantify changes in total cellular SUMO levels upon exposure to heat shock (43°C), the proteasomal inhibitor MG132, and the translational inhibitor cycloheximide (CHX). This was needed because Immunoblot analysis, the most used technique to detect SUMOylation, might not provide accurate SUMO quantification given that the conjugated and free forms of SUMO have very different molecular weights. This fact makes it near impossible to obtain quantitative transfers and retention of both forms during electroblotting. Dot blots are more likely to provide an accurate quantification of total SUMO levels because they are not affected by the protein's molecular weight. The membrane is imprinted with wells in which the various cell extracts are directly spotted onto, followed by immunodetection of SUMO1. Our results, obtained using GAPDH as housekeeping gene control, did not indicate the triggering of an increase in cellular SUMO1 levels upon heat shock (43°C for 1h). Therefore, either the current heat shock protocol is not effective or GAPDH levels are also increased during heat shock and a different housekeeping gene control should be utilized.

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High-Throughput Silver Nano Cluster Beacons Activator Sequence Selection

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Silver NanoCluster Beacons (NCB) are an outstanding activatable probe. Interacting with a proximal DNA sequence termed activator sequence, a non-emissive silver nanocluster can be activated and emit a fluorescence signal that can be tuned from visible to near-infrared range. A high-throughput activator sequence selection on next-generation sequencing chip using Chip-Hybridized Association Mapping Platform (CHAMP) facilitates us to study the interaction between NCB and millions of DNA sequences simultaneously.

We evaluate our system by epifluorescence microscope and apply CHAMP algorithm to register the images. We obtained several used chips from UT Facility, to validate our setup. The Graphical User Interface (GUI) we designed can make Micro-Manager control the stage and take images automatically. After we add handler sequences linking with activator sequence, NCB can hybridize with the handler sequences and generate fluorescent signal.

The results of alignment are obtained from the sequencing file coordinates, termed fastq data. The best alignment rate for Atto 647-PhiX label is 84% for a specific row or 70% in total. With the GUI facilitating image acquisition, we are able to record a great amount of image data. However, currently, the signal to noise ratio is not acceptable for us to do the alignment for NCB handler-PhiX label.

Proper alignment of fluorescent images is crucial for optimal design and quantification of NCB. We performed a high-throughput selection algorithm on our setup using Atto 647 dye. Due to the poor signal-to-noise ratio for NCB-handler-PhiX labeling, the NCB alignment feasibility still needs to be tested.

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Acid Sensing Ion Channel 1 Effect On The Systemic Vasculature In Response To Angiotensin II

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The acid sensing ion channel 1 (ASIC1) is part of the amiloride-sensitive epithelial sodium channel superfamily. Activation of ASIC1 results in Na+ and Ca2+ influx in both vascular endothelial and smooth muscle cells. Ca2+ is involved in numerous cellular processes including contractility and is important for the control of vascular tone. Recent data from our laboratory shows that ASIC1 null mice are protected from the development of angiotensin II-induced hypertension, however the mechanism by which ASIC1 contributes to angiotensin II-induced hypertension is unknown. Based off preliminary studies, we hypothesize that ASIC1 mediates vascular smooth muscle cell (VSMC) Ca2+ influx and contributes to angiotensin II-induced vasoconstriction. To test this hypothesis, we will measure intracellular Ca2+ ([Ca2+]) using the ratiometric Ca2+ indicator, fura2-AM, in response to different concentrations of angiotensin II (10−7 - 10−5 M) in VSMC from wild type and ASIC1 knockout mice. We will additionally measure angiotensin II-induced contraction in vascular rings from wild type and ASIC1 knockout mice. After experimentation, we concluded that ASIC1 contributes to Ang II-induced Ca2+ influx in VSMC. However, ASIC1 does not contribute to Ang II-induced vasoconstriction in isolated pressurized mesenteric arteries. The lack in response of Ang II in isolated arteries may be due to the role of ASIC1 in other cell types. For example, in mesenteric arteries, ASIC1 contributes to vasodilation.

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Optimizing Lipid Microbubble Synthesis and Conjugation

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Microbubbles are a versatile tool used for theranostic purposes. A microbubble is a gas core stabilized by either a lipid, protein, or polymeric shell. When used in ultrasound imaging, they serve as a contrast agent, while more recently, microbubbles have been used for targeted drug and gene delivery via the use of conjugated functional groups as well as magnetic nanoparticles. In this study, we tested different ratios of lipids to optimize microbubble size and signaling. Furthermore, we studied conjugation efficiency of PLGA nanoparticles onto microbubbles via the use of biotin and avidin bindings. Optimized microbubbles were synthesized to be conjugated with nanoparticles at different mass ratios. Microbubbles synthesized at 6:1 and 5:2 ratios of DPPC:DPSE showed the best signal stability over time since they were able to maintain relatively high signal retention for longer than the other types of synthesized microbubbles. One ratio yielded more microbubbles, however, the other ratio returned a higher conjugation efficiency with nanoparticles due to the fact that this type of microbubble had twice as much biotin tags. More studies will be conducted to increase nanoparticle conjugation efficiency, as well as to investigate nanoparticle conjugated microbubbles' effect on ultrasound imaging.

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Identifying ErbB proteins as potential receptors for nephronectin during mouse corneal development

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Corneal defects are a major cause of blindness, but treatment options remain limited. Understanding the molecular processes involved in corneal development may provide insights that result in new treatments. Corneal development is an intricate process that involves migration, proliferation, and differentiation of embryonic neural stem cells known as neural crest cells. However, very little is known about the molecular mechanisms involved in these processes. We identified novel expression of Nephronectin (Npnt), an extracellular matrix protein, in the developing cornea. The current study is to determine whether Npnt signals through ErbB proteins (ErbB1, ErbB2, ErbB3) during corneal development. To test the hypothesis that neural crest cells respond to Npnt signaling through ErbB receptors during corneal development, we isolated cDNA from ocular tissues, then identified the expression of the ErbB genes by reverse transcription polymerase chain reaction (RT-PCR), and then determined their localization in the cornea by in situ hybridization. Analysis by RT-PCR indicates that ErbB1, ErbB2, and ErbB3 transcripts are expressed during ocular development. Next, we synthesized RNA probes using a cloning vector to analyze their spatial expression on paraffin embedded embryonic corneal sections. Our results show that ErbB1 is expressed in the presumptive corneal stroma and epithelium, suggesting a potential role of Npnt/ErbB1 signaling during cell migration, proliferation, or differentiation. ErbB2 and ErbB3 are localized in the corneal epithelium, indicating a potential role in proliferation. Combined, our data indicate that Npnt signaling through ErbB receptors may play crucial roles during corneal development.

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Device That Creates Core-shell Yarns For Biomedical Applications

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Composite materials have become of great importance in the biomedical field due to their vast applications. Core-shell yarns, i.e. Nanofibers fabricated with electrospinning, have proven useful as a result of their ability to mimic the human Extracellular Matrix (ECM). The objective of this summer project was to design and prototype a mechanism to fabricate composite core-shell yarns. The automated device facilitates the wrapping and coating of the core with electrospun fibers, thus creating a core-shell yarn with multiple biomedical applications

Observations acquired in the first three trials were concerning the electrospun material hardly surrounding the core completely while approaching the center. However, the fibers were spun tight around the core near the ends. This led to the conception that if the brush diameter increased then the polymer will coat the material around the core more homogeneously. For time constraints, we decided to decrease the distance between the two brushes in the last trial. This showed that increasing the ratio of brush diameter to core length will produce the highest quality of coating surrounding the core.

Through many alterations we created a mechanism that was found to have a tighter and more efficient method of coating when increasing the brush size. Construction of the mechanism now allows for electrospun material to coat any yarn-like material for biomedical applications. The developed device enables the laboratory to continue experimentation with specific biomedical applications. Future work would involve updating the materials of the model and making different sized detachable brushes.

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Biomedical Education 2

Negative Mentoring in Undergraduate Research in the Life Sciences

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Undergraduate research experiences (UREs) typically involve an undergraduate researcher working with a research mentor, such as a graduate student, postdoctoral associate, or faculty member. Studies of UREs indicate that undergraduate students benefit from these experiences, yet studies of the mentoring component of UREs have focused solely on the positive elements. Despite the documentation of negative mentoring in graduate education and in the workplace, there has been little, if any, study of this phenomenon in UREs. To explore whether and how negative mentoring occurs in UREs, we conducted a phenomenological study of negative mentoring in undergraduate research in the life sciences. Specifically, we conducted semi-structured interviews with a national sample of undergraduate students (n=39) from diverse institution types who had participated in research in the life sciences and had at least one experience that they perceived as negative. We conducted content analysis of the interviews utilizing theories of negative mentoring in the workplace, abusive supervision, and workplace incivility and analyzed the interviews to find themes specific to negative mentoring in UREs. The results of these analyses have been used to generate a typology of negative mentoring in UREs which showcase the facets of either actively harmful mentoring or the absence of positive mentoring from a vocational and psychosocial perspective. In the future, we aim to use this typology to create a quantitative measure of negative mentoring in undergraduate research in order to assess its prevalence and impact and test the effectiveness of interventions designed to reduce or prevent negative mentoring.

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