Life-Health Sciences Internship Program at IUPUI

Spring 2015 Poster Session

Friday, April 10, 2015
3:00 PM—5:00 PM
VanNuys Medical Science Building Atrium
Welcome to the IUPUI Life-Health Sciences Internship Program Spring 2015 Poster Session.

The Life-Health Sciences Internship Program connects IUPUI life and health sciences undergraduates with research internships on and near the IUPUI campus. This program allows students to explore their career objectives and future career pathways, while also fostering valuable professional connections between students and faculty and staff. The students belong to a community of interns and mentors who support one another throughout the research experience and beyond. This program is funded by an IUPUI Commitment to Excellence grant and the Deans of the Schools of Science, Engineering & Technology, Health & Rehabilitation Sciences, Liberal Arts, Physical Education & Tourism Management, Social Work, and University College.

Life-Health Sciences Internship students represent 18 different majors spanning seven schools on the IUPUI campus. Many of these undergraduates have career goals involving research, medicine, dentistry, occupational therapy, physical therapy, and pharmacy. These internships are an excellent stepping stone for future research and graduate study.

Mentors represent the Indiana University School of Medicine, the Indiana University School of Dentistry, the Indiana University School of Health and Rehabilitation Sciences, Richard M. Fairbanks School of Public Health, and research departments in Indiana University Health. These professionals are providing invaluable experiences for undergraduate students and mentoring the next generation of scientists, researchers, and health professionals.

This year we have expanded the poster session to include LHSI alumni who have continued their work and poster awards from the LHSI Alumni Council to honor the best posters and speeches by our current interns. This program includes summaries of the posters presented and work completed by our interns. Thank you for joining us today!

Brandi Gilbert
Director, Life-Health Sciences Internship Program
Thank you to our 2014-2015 participants:

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Targeting the role of tyrosine in Amot protein-lipid binding events

Amot proteins have been shown to control cell proliferation and differentiation and can selectively bind with high affinity to phosphoinositol containing membranes. This binding event is linked to endocytosis, changes in cellular polarity, and apical membrane sequestration of nuclear transcription factors associated with development of cancer phenotypes. Although the lipid selectivity of the protein has been well characterized, the mechanisms involved in the Amot coiled-coil homology domain (ACCH) binding these membranes are not yet known. The fluorescence properties of the ACCH domain were used to characterize the binding event, however it became clear each of the five native tyrosines proximity to membrane might differ based on fluorescence resonance energy transfer experiments with fluorescently tagged lipids. A variety of short peptides correlating to the amino acid sequence of Amot surrounding these tyrosines were assayed and observed in different membrane mimicking environments to determine if each tyrosine had the ability to bury into the hydrophobic region of the membrane (alcohol study), or simply interacted with the hydrophilic head groups (liposome study). Interactions were characterized by shifts in absorbance, excitation and emission scans peaks. A characterization of these shifts with respect to what is seen with the various tyrosine-phenalanine mutants will further our understanding of whether each tyrosine is buried within the protein or interacts with the membrane.

Effect of mir21 in Connexin43 Deficient MLO-Y4 Cells in Mice

Connexin 43 (CX43) is a gap junction protein that affects a cell's signaling pathway through intercellular channels, both in mice and humans. Osteocytes are regulated by different pathways and molecules. Deletion of CX43 in MLO-Y4 osteocytic cells results in increased cell death, apoptosis, similar to findings in old mice and humanism. In a previous study, our laboratory concluded that deletion of CX43 from osteocytes in mice decreases the levels of pro-survival microRNA mir21, which suggested that mir21 could be involved in increased apoptosis in MLO-Y4 cells lacking CX43. mir21 decreases the expression of the protein PTEN, a phosphatase that reduces the phosphorylation of the pro-survival kinase Akt, thereby inactivating it. Therefore, CX43 deficient cells should have a decreased level of mir21, an increased level of PTEN, and reduced pAkt. In order to decrease osteocyte apoptosis, mir21 mimic was introduced which could reverse the increased apoptosis of CX43-deficient MLO-Y4 cells, suggesting that osteocytes die in the absence of CX43, due to reduced mir21 expression. As an expected consequence of mir21 reduction, western blot analysis showed that the protein level of PTEN was increased in MLO-Y4 cells lacking CX43, as revealed by a 3X fold higher level of PTEN corrected by beta-actin (used here as a housekeeping gene). These findings raise the possibility that mir21 could be a target to improve aging-induced bone fragility, and suggest that osteocytic pathways are involved in skeletal changes in old mice and human.
Repellent Transcranial Magnetic Stimulation in Schizophrenia with Emphasis on First-Episode Psychosis.

Schizophrenia is a chronic and disabling illness associated with impairments in areas of social and vocational functioning and independent living. Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive intervention that utilizes the application of a repetitively pulsed magnetic field over the scalp to induce an electric field within a discrete area of the cerebral cortex which results in altered neuronal activity where the rTMS is applied. Throughout schizophrenia literature, rTMS has been applied with aspirations on alleviating auditory hallucinations, positive symptoms, and negative symptoms associated with the disease, however there is a decrease in the amount of research conducted where rTMS is applied to study cognition. The literature presents several inconsistencies; these inconsistencies may be attributed to the fact that chronic schizophrenia patients tend to have more frequent and severe comorbidities, longer durations of antipsychotic treatment, and greater severity of illness. The absence of literature on cognition in schizophrenia and inconsistencies in research in chronic schizophrenia indicate a need for research on cognition in first-episode psychosis (FEP) using rTMS. In our present study the primary aim is to determine if rTMS is effective in improving cognition in individuals with FEP. Secondary aims include determining if rTMS is effective in improving general symptoms and function. It is hypothesized that cognition and general symptoms will improve with active versus sham rTMS administration. Final results are not presented as this double-blind study is still ongoing. If effective, rTMS may represent a preventative treatment for the development of social and vocational impairments in FEP.

Adipose Stromal Cells Ameliorate Renal Injury and Decrease Capillary Damage Following Ischemia-Reperfusion Injury

Acute kidney injury (AKI) is the abrupt loss of kidney function, and diagnosed on the basis of abnormalities in urine and blood composition. We have convincing evidence to prove that rats with induced AKI via ischemia/reperfusion (I/R) had permanent damage to capillary density, tubular epithelium, and renal endothelium. Our interest lies in the timeline and degree of natural repair of the injured kidney in restoration of lost endothelium and revascularization of the damaged tubules. Preclinical studies suggest that exogenous mesenchymal stem cells (MSC) facilitate recovery as a catalyst for restoration and revascularization in the damaged area. Human adipose stromal cells (hASCs) are derivatives of MSCs, unique for their potential to differentiate into mesodermal cells and tissue. Here, we hypothesize that hASCs facilitate recovery of the renal function, at least in part, by stimulating revascularization of the affected area and/or preservation of capillary density. To test this hypothesis, Male Sprague-Dawley rats were subject to bilateral I/R injury for 40 minutes. At the time of reperfusion, either $2 \times 10^6$ human adipose stromal cells (hASCs) or control media was administered via a suprarenal aortic injection. Serum creatinine values collected at days 1, 2, 4 and 7 time points post-surgery indicated that the hASCs significantly improved epithelial and vascular conditions. Our results indicated that MSCs improve injury by preserving capillary density and reestablishing renal function.
Intern: Brittany Baker
Major: Neuroscience, Medical Humanities

Mentor: Debra Hickman
Department: Laboratory Animal Resource Center

Cage Change Influences Cardiovascular Function and Anxiety-Like Behaviors in the Mouse

Basic husbandry procedures are capable of inducing certain stress-like responses as well as influencing the physiology in mice. The objective of this study was to assess alterations in cardiovascular function and behavior of individually housed C57BL/6 male mice with telemetry in response to some standard husbandry manipulations. In the study, five mice were evaluated to determine the effects of cage change and blood draws on mean arterial pressure (MAP) and heart rate. Behavioral data was also collected by video to monitor the correlation between anxiety-like behavior and the timing of husbandry manipulation. We hypothesized that MAP, heart rate, and anxiety-like behaviors would increase in response to cage change and blood draw. The implanted telemeters collected data every 10 seconds and were enabled at least two hours prior to manipulation to determine a baseline physiology. Post manipulation, the telemeters were enabled for at least two hours for blood draw and six for cage change. The results indicated that heart rate and anxiety-like behaviors increased, however, MAP remained constant due to the maintenance of homeostasis. This provides evidence that the timing of cage change and blood draw can influence behavior and physiological experimental results.

Intern: Macy Ballard
Major: Psychology

Mentor: Silvia Bigatti and Katrina Conrad
Department: Public Health, Social and Behavioral Sciences

Sparks and Resilience in Indianapolis Latino Youth

Acculturative Stress (AS) can occur when a person balances between two cultures. High amounts of AS are related to a higher likelihood of developing depression. Resiliency has been shown to help protect against depression. Therefore, resiliency building can help youth experiencing AS develop the skills to fight depression. A summer camp was conceptualized as a resource for Latino teens in the Indianapolis area to learn such resiliency skills. According to Dr. Peter Benson, children have a “spark,” a talent that drives their behavior. When nurtured, sparks grow into passions, hobbies, and even careers. Before camp, participants sent in applications answering brief essay questions, from which such sparks were identified. Interestingly, participants had an alarming number of positive sparks associated with serving others, making an impact on the world, and a commitment to loved ones. The evaluation also included a version of the California Healthy Kids Survey (HKS) to measure school, community, internal, peer, and home protective factors. Interestingly again, many positive traits were present before treatment, such as empathy, goal setting, and service. About 90% of participants planned to graduate high school and pursue some form of higher education. This presentation will focus on descriptives between the HKS and the sparks identified from baseline. In spite of all the positive attributes found, Indiana Latino youth appear to be at a higher likelihood of developing depression. Future analyses will study correlations between these measures and AS in regards to depression.
Feasibility and Participant Value of Community-Based Adapted-Group Yoga in People with Acquired Brain Injury: Preliminary Data

Background: Acquired brain injury (ABI), is a devastating medical event leading to long-term physical impairments. Due to these long-term impairments and short rehabilitation stays, people with ABI need to be engaged in community-based exercise. Unfortunately, adapted programs are rarely available. Purpose: The purpose of this study was to explore the feasibility of implementing an adapted-yoga class in the community. The aims were to describe perspectives on: 1) the value of an adapted-yoga program and 2) ability to continue yoga after participation in an adapted class. Methods: This was a pilot, feasibility study. Participants were recruited through local rehabilitation programs and the YMCA. Participants attended an adapted-yoga class (2X/week for 8 weeks) at the local YMCA. After the class, participants were invited to attend a focus group/semi-structured interview where feasibility data were collected with a standardized list of open-ended questions. Responses were recorded, transcribed, and analyzed with a content analysis approach. Results: Nine participants were recruited. Seven (78%) completed the class and participated in a focus group/semi-structured interview. The average age of the sample was 52 years. Five (71%) were male, and 4 (57%) had left hemiparesis. The data suggest that the adapted-yoga class was valued based on; 1) benefits of participating, and 2) willingness to pay a fee for a similar class. The ability to continue yoga after the class was also suggested by the data. Conclusion: The adapted-yoga class had value to the participants and was feasible in this setting.

A Comparison of the Prediction Error of Two Structure-Function Models of Glaucoma Progression in Patients with Ocular Hypertension

Purpose: Combining structural and functional data may improve our ability to predict glaucoma progression. In this analysis performed on prospective data collected in an observational clinical study, we compared the prediction accuracy of two glaucoma progression models that use structural and functional data. Results: The RMSPE of the DSFMS was 12.0% (10.8%−13.5%); significantly lower than that of the BLRMS, with a RMSPE of, 16.8%; (14.6%−18.9%). The DSF model yielded better prediction accuracy in 62.3% of eyes compared to BLR. When predicting structure, the median RMSPE of the DSFRA was 2.1% (2.0%−2.4%); significantly lower than that of the BLRRRA, with a RMSPE of 2.5% (2.3%−2.9%). The DSF model yielded better prediction accuracy in 56.3% of eyes compared to BLR. Conclusion: Overall, the DSF model had lower prediction error than the BLR model in this sample of patients with ocular hypertension. The DSF model also had lower prediction error in a larger number of eyes compared to BLR. Future work will focus on developing methods to detect progression in the two-dimensional structure-function space.
Evaluation of Functional Efficacy of Potential Anti-Inflammatory Agents

Acute inflammation is the protective response to infection or trauma and resolves once the initiating stimulus is removed. However, the primary stimulus is often unknown and difficult to remove in chronic inflammation associated with many diseases including cancer and Alzheimer's disease. Mechanistically chronic inflammation is the end result of a complex cascade of signaling events that activate latent transcription factors such as nuclear factor-kappa B (NF-κB). In resting cells, the NF-κB remains in the cytoplasm as an inactive complex of p50 and p65 subunits bound to the IκB inhibitory proteins. Following activation the p65 subunit is released to the nucleus and transactivates inflammatory mediators that provide a feed-forward loop for amplification of the initial response. Glucocorticoid induced leucine zipper (GILZ) is an anti-inflammatory protein that binds and prevents nuclear translocation of NF-κB-p65. The interface between the GILZ and the p65 proteins consists of the proline rich region of GILZ and the transactivation domain of p65. We hypothesize that a GILZ mimic can block activated p65 and suppress inflammation we designed peptide analogs of the proline rich region of GILZ, called GA as potential drug like agents. Human macrophage like THP-1 cells stimulated with lipopolysaccharide or IFN-gamma were cultured at 37°C in the presence of different GA at varying concentrations (125μg/ml-1mg/ml) for 24 hours. Supernatant was assessed for cytokines IL-6 and IL-12 by enzyme linked immunosorbent assay. GA1, GA3 and GA4 treatment suppressed IL-6 and IL-12 cytokines in activated THP-1 cells. This suggests that the GA could represent potential anti-inflammatory drugs.

Role of Klotho in the Parathyroid Glands

Fibroblast growth factor 23 (FGF23) is a phosphaturic hormone produced in the bone. FGF23 primarily acts on the kidneys and decreases serum levels of phosphate and 1,25-dihydroxyvitamin D. In order for FGF23 to have effect on target organs, it must bind to proteins known as FGF receptors (FGFRs). FGF23 also requires a co-factor, encoded by the Klotho gene, to increase the FGFR’s affinity for FGF23, and its expression provides tissue specificity for FGF23 action. Klotho is expressed in the parathyroid glands, which secrete parathyroid hormone (PTH), a hormone regulating phosphate and calcium homeostasis. It has been speculated that FGF23 suppresses PTH expression. However, patients with chronic kidney disease (CKD) have high PTH, despite elevated levels of FGF23. To determine FGF23’s effect on PTH secretion, the Klotho gene was deleted in the parathyroid glands of the mouse model of CKD, juvenile cystic kidney disease (Jck). The mice with parathyroid-specific Klotho knockout and littermate controls were sacrificed at 12 weeks of age, and their serum levels of blood urea nitrogen (BUN), creatinine, alkaline phosphatase, calcium, phosphorus, and FGF23 were measured. BUN and creatinine levels were elevated in Jck mice, indicating reduced kidney function. In addition, the male Jck mice weighed significantly less than the normal controls, beginning at 8 weeks of age. Jck mice, regardless of the Klotho status, had increased calcium and FGF23 levels, compared to normal controls. Importantly, loss of Klotho tended to reduce the increase in calcium and FGF23 and prevented the development of hyperphosphatemia in male Jck mice. In contrast, loss of Klotho did not affect any measured parameters in normal controls. These data indicate that Klotho likely affects sensitivity to FGF23 in parathyroid glands and may have a regulatory effect on the
Physical Predictors of Driving Performance

It is estimated that nearly 20 million drivers in the United States are over the age of 70. This portion of the population is approximately seven times more likely to be involved in automobile crashes, which result in injuries and fatalities. Individuals who experience declines in vision, cognition, motor skills and other areas of functioning also experience an increased safety risk among drivers. As the population continues to age, it is becoming more important to accurately and successfully identify at-risk-drivers. Driving assessment tests such as the Mini-Mental State Exam, visual acuity, and rapid pace walk are used to identify cognitive, visual, and physical predictors of driving performance. Higher accuracy in assessing driving performance decreases the likelihood that drivers will experience the negative impact of driving cessation/reduction. The goal of this study was to accurately identify specific physical predictors of driving performance among at-risk-drivers through data collection and referencing existing literature. Over the course of this study I was able to actively participate in creating a study design, literature review, and data entry/collection. The results of this study will help to more accurately assess driving performance as well as making driving rehabilitation services more effective among at-risk-drivers.

Cognitive Substrates in Relation to Predicting Driving Outcome in Older Adults

In 2012, 5,560 older drivers (aged 65 or older) were killed and 214,000 were injured in automobile crashes. The rate of driver fatalities for this age group has declined by 15 percent since 2003. To insure the rate continues to decline, research must be completed to guarantee that the substrates currently being used to assess older adults’ ability to drive are reliable and valid. Substrates are divided into three domains: cognitive, physical, and vision. The goal of this study was to review published literature related to the cognitive substrates used to assess older drivers. Cognitive substrates that were reviewed include the Mini-Mental State Exam (MMSE), Trail Making Part A and B, Clock Drawing Task, Useful Field of View (UFOV), and the Maze Test. Many of the articles reviewed demonstrated conflicting results, leading to the implication that some tests, such as the Trail Making Part A and the Clock Drawing Task, are unreliable in predicting the driving performance of older adults.
Reduced skeletal muscle function is associated with decreased fiber area and increased connective tissue in a rat model of progressive kidney disease.

Sarcopenia plays a role in the functional decline commonly observed in Chronic Kidney Disease (CKD) patients, but the pathophysiology of muscle mass/strength changes remains unclear. The purpose of this study was to characterize muscle properties in a rat model of spontaneously progressive CKD. Leg muscle function and serum biochemistry of male Cy/+ (CKD) rats and their non-affected littermates (NL) was assessed in vivo at 30 and 35 weeks of age. Architecture, histology, and fibrosis of extensor digitorum longus (EDL) and soleus (SOL) muscles were assessed ex vivo at the conclusion of the experiment. The tested hypothesis was that animals with CKD have progressive loss of muscle function, and that this functional deficit is associated with loss of muscle mass and quality. From 30 to 35 weeks of age, decreased peak ankle dorsiflexion torque and time to maximum torque with longer half-relaxation time compared to NL was shown. Mass, physiologic cross-sectional area, and fiber type (myosin heavy chain isoform) proportions of EDL and SOL were not different between CKD and NL. However, the EDL of CKD rats showed reduced cross-sectional areas (CSA) in all fiber types while only MyHC-1 fibers were decreased in area in the SOL, with significantly higher proportion of connective tissue in both muscles. The results of this study demonstrate that muscle function progressively reduces in the CKD rat model, with only diseased muscles showing reduction in individual fiber CSA. This suggests that the uremic sarcopenia is related to increased muscle fibrosis.

Marion County trends in Suicidality due to Drug Overdose

Nearly 30,000 lives are lost to suicide in the United States each year, resulting in many more lives affected as individuals cope with the loss of loved ones. This suicide rate is almost twice as high as the number of deaths from homicide each year. Lack of evidence during investigation can result in possible suicides being ruled as accidental deaths. Suicides must have some form of verbal or written communication to indicate that the deceased did intend on taking their own life. Drug overdose has become a leading cause of death in Indiana and is highly related to incidences of suicide. This study was done to evaluate the incidence of suicide in the prescription drug deaths for Marion County, Indiana. For this research, 5 years (2009 through 2014) of death records were compiled from the Indianapolis Marion County Coroner’s Office. In these records, it was determined that a total of 621 drug overdose deaths occurred over the 5 year period. Delving further, we found that 542 cases were ruled as accidental, 6 were ruled as suicide, and 73 were ruled as undetermined. Cases declared undetermined lacked sufficient evidence to support suicidal ideation or probable cause for accidental death. In conclusion, our data from overdose, combined with data from blunt force trauma, showed that the incidence of suicide increased over a five year period (2009 through 2014) compared to the Indiana study on suicidality from 2001-2005.
The Sesn2 gene is regulated by metformin and resveratrol

Sestrins (Sesns) are a family of stress-inducible proteins that have been shown to serve an important homeostatic function in the regulation of physiological pathways such as lipid and glucose metabolism. Though how these sestrin genes are regulated is not clear. In this study, we attempted to investigate the regulation of the Sesn2 gene. Hepatoma cell line HepG2 was used as a cell model to examine the effects of metformin, the most commonly prescribed diabetes drug, and resveratrol, an anti-oxidative stress compound on the regulation of Sesn2 protein. The western blot analysis indicated the 24-hour treatment with resveratrol increased Sesn2 protein levels. Moreover, the 48-hour treatment showed increased levels of Sesn2 protein with treatment of resveratrol and metformin. Our data suggested that these compounds can enhance the Sesn2 function. To further investigate the molecular mechanism of Sesn2 gene regulation, we also cloned the 2 kb promoter of the Sesn2 gene into a luciferase reporter system. This should allow us to assess whether metformin and resveratrol regulate the Sesn2 gene directly or indirectly. In conclusion, our data reveals that Sesn2 can be regulated by metformin and resveratrol in liver cells. The findings suggest a critical role of Sesn2 in liver metabolism as metformin and resveratrol have been shown beneficial for diabetes and fatty liver disease.

Intern: Emilee Freeland
Major: Exercise Science
Mentor: Niki Munk
Department: Health and Rehabilitation Sciences

Massage Therapy Combined with Components of Mirror Therapy is Helpful for a Man with Phantom Limb Pain: Case Report

Phantom limb pain (PLP) is a common issue for amputees and is difficult to treat. No therapy (including pharmacological) is considered particularly effective. Massage therapy’s (MT) efficacy for pain is established and we were interested in “applying” MT on a phantom limb using Pfluger’s law of symmetry and components of mirror therapy. Methods: Single-subject ABA withdrawal experimental case series. Each phase of the study was 4-weeks long. Study phase B included bi-weekly MT combined with components of mirror therapy allowing an image of participant’s intact leg getting a massage to be seen in place of the missing leg. To date, three lower-limb amputees have completed the study; we present results of one participant: 44-year-old male. Outcomes/Measures - PLP severity measured with visual analogue scales collected 2/week and averaged for each phase. PLP intensity and interference measured with Brief Pain Inventory collected at baseline and each phase’s end along with SF-36v2 (health-related quality-of-life). Results: Participant reported that overall, the treatment was beneficial for his PLP and that continuing treatment would improve already meaningful outcomes. Baseline PLP severity (current PLP=10.3, average severity=39.9, worst episode=54.9) decreased during treatment phase (0.6, 8.8, 17.6, respectively) and maintained during the withdrawal phase (3.9, 12.1, 19.7, respectively). Each time treatment was administered when PLP was present, post-treatment PLP=0. PLP intensity decreased and maintained after treatment phase. Conclusion: MT combined with components of mirror therapy was helpful for this individual’s PLP. Successful management of PLP is elusive and effective non-pharmacological treatment options should be explored and made available.
The impact of intrauterine diabetic exposure on TNF-α signaling in endothelial colony forming cells.

Children born to diabetic mothers have an increased risk of developing type 2 diabetes, obesity, metabolic syndrome, and hypertension. Critical components of vascular health, endothelial progenitor cells are studied in our lab as indicators of the severity of fetal diabetic exposure during pregnancy. Specifically, we determined that endothelial colony forming cells (ECFCs) undergo premature senescence, have altered proliferation, and exhibit disrupted vessel formation as a result of intrauterine diabetic exposure. Since inflammation is often elevated in individuals with diabetes, we assessed the response of ECFCs from diabetic and non-diabetic pregnancies to a common inflammatory cytokine, tumor necrosis factor alpha (TNF-α). The goals of this study were to identify if TNFR1 expression is altered in ECFCs exposed to intrauterine diabetes, and whether or not downstream TNF receptor signaling is altered in response to TNF-α. We hypothesized that TNFR1 is upregulated in ECFCs exposed to intrauterine diabetes, resulting in increased activation of p38MAPK and contributing to premature senescence. Protein lysates were collected from cultured healthy and diabetic ECFCs and Western blotting was used to examine protein levels of TNFR1 in whole cell lysates as well as subcellular fractions. Additionally, ECFCs were treated with TNF-α, and levels of phospho-p38 were determined by Western blotting. Our preliminary results indicate that TNFR1 expression is not altered in ECFCs exposed to intrauterine diabetes. However, phosphorylation of p38 may be elevated in response to TNF-α treatment in ECFCs exposed to intrauterine diabetes.

Experimental testing of Drug to Determine Efficacy of Suppression of TTR Gene Stopping Progression of Familial Amyloidosis Polyneuropathy.

Familial Amyloidosis Polyneuropathy (FAP) is a progressive disease where a mutation in the TTR gene creates Amyloid deposits which cause nerve disease. It is a rare disease that has over 100 different mutations and is estimated to affect 10,000 people in the world. Currently, there is no cure and very little treatment for any of the FAP mutations. This study is an experimental drug study for the ISIS formula to determine if it is viable as a treatment for all mutations of FAP. The drug is an antisense drug, and its purpose is to block the translation of the mutated segment of the TTR and stop the progression of the TTR mutation rather than cure the disease. A world-wide scale clinical trial is being done on this drug, measuring both its effectiveness in FAP patients and its safety with prolonged use. Patients are followed and tested along a 65 week period to measure the progression of the disease. 2/3 of patients receive drug while 1/3 of patients receive a placebo. This study is continuous and double-blind and therefore has no concrete results as of yet. Previous trials with the drug in rats, primates, and healthy human subjects suggests that the drug does safely work in suppressing the TTR gene with prolonged usage.
Comparing refractive error distribution in children with Intermittent Exotropia from the Chinese and American Non-Chinese ethnicity

Children with Intermittent Exotropia (IXT) in the West are often emmetropic or low hyperopic. It is possible that Chinese children with IXT are more myopic than children with IXT in the western countries. This study compared the refractive error distribution at the age of detection in children with IXT in Hong Kong to children with IXT in Indiana, USA. Retrospective cohort study of children with IXT from Hong Kong (Chinese ethnicity) and Indiana (American Non-Chinese ethnicity: 85% Caucasian and 15% of other races, excluding Chinese). Eligibility criteria included: 3 to 15 years old, diagnosed with IXT, no prior surgery, no Down syndrome or other systematic or genetic conditions, and birth age >36 weeks. Cycloplegic refractive errors at the age of detection culled from medical records were converted to a spherical equivalent (SEQ) in diopters (D). Both SEQ and CYL were analyzed for two age subgroups: a 3- to 7-year-old subgroup and an 8- to 15-year-old subgroup. To compare the SEQ difference between the two groups, an independent t-test was used. On average, SEQ is more myopic in the Chinese group than in the American non-Chinese group. The SEQ of Chinese children in two age subgroups were all significantly more myopic than that of American non-Chinese Children (p<0.05, see Table 1). However, there was no significant difference on the CYL between groups (p=0.6). Compared to American Non-Chinese children with IXT, Chinese children with IXT are more myopic. Such distribution may be associated with the high prevalence of myopia in Chinese ethnicity.

Increasing the Number of Physicians in Rural, Underserved Indiana Counties

In the third year of medical school, medical students undergo the process of choosing where they will participate in clerkships for a specific area of medicine. For the IU School of Medicine campus in Indianapolis, the majority of students try to complete their clerkships within Indianapolis itself. While these students are receiving a well-rounded medical education, it is known that the place where students decide to do their clerkships can influence where they complete their residency, and therefore, where they practice medicine. As of right now, the clerkship program offers sites within underserved, rural populations of Indiana. However, the problem with getting the medical students to choose these sites may be due to the newness and unfamiliarity of territory which can make the decision to go there less likely. The goal of this project is to increase the number of students that choose to complete clerkships in underserved areas of Indiana. This will occur through the establishment of an interactive map tool of Indiana that will allow medical students to hover over any doctor’s office, when choosing their clerkship, and see the top health problems in that county, the personal characteristics of the doctor at the site, and everyday-living details. Through this interactive map, the unfamiliarity of the clerkship site will diminish making it more likely for the student to choose this site. In turn, the student may be more likely to come back to the site to complete their residency and, possibly, set up as a practicing physician.
Whole Slide Image Analysis Quantification Using Aperio Digital Imaging in a Lung Cancer Mouse Model

More people in the United States die from lung cancer than any other type of cancer. Most mouse model studies have been set up exposing mice to mainstream smoke for periods up to 30 months. In this study, we used Aperio digital Imaging to evaluate early changes in respiratory bronchial epithelium at a six month time frame. The mice were exposed to 5 hours a day, 5 days a week in a TE-10 smoking chamber. The cigarettes used are 1R3F reference cigarettes. By light microscopy, the smoking group had a lower bronchiolar epithelium height compared to the non-smoking controls. Major histological changes in the smoking group had a flattening of the bronchial epithelium in the small and medium bronchioles compared to the non-smoking control group. By visual examination, bronchial epithelium had become flattened in the smoking group. Using quantitative image analysis, the data obtained from the Aperio Positive Pixel Imaging confirmed the above histological changes. In conclusion, we were definitively confirm microscopic changes caused by cigarette smoking at this early time frame using Aperio Positive Pixel Image Analysis.

Osteocyte-specific Overexpression of Human WNT16 Increases both Cortical and Trabecular Bone Mass and Improves Bone Strength in Mice

Osteoporosis is a common bone disease that affects 50% of women and 25% of men ages 50 and above, resulting in a low bone density and increased susceptibility to fracture. Our previous genome wide association study reported the association of WNT16 with low bone mineral density (BMD) and risk of fracture. We created transgenic (TG) mice that overexpressed WNT16 in osteocytes in both male and female for further understanding the gene. We compared bone density, micro-architecture, and strength between wild-type (WT) and TG mice through the use of DXA, micro-CT and femur biomechanics tests. Compared to WT mice, WNT16-TG mice exhibited significantly (p<0.005) higher whole body and spinal BMD at six and twelve week of age in both genders. Micro-CT analysis revealed significantly (p<0.0002) higher trabecular bone volume at distal femur and significantly (p<0.05) greater cortical bone thickness and area in twelve-week-old TG mice compared to WT littermates. Additionally, female TG mice presented significantly (p<0.05) greater femoral ultimate force, stiffness, yield force, and energy to ultimate force where male TG mice displayed an inclination for higher biomechanical parameters compared to sex-matched WT mice. Our results indicate that osteocyte-specific overexpression of WNT16 increased whole body and spinal BMD, heightened cortical and trabecular bone volume, and improved bone biomechanical properties in both male and female. The WNT16 molecule will likely be an excellent target for pharmaceutical development of drugs to treat osteoporosis and other low bone mass conditions.
Role of Kalirin Domains on Pyk2 Phosphorylation in Osteoblasts

Bone is constantly being remodeled by osteoblasts and osteoclasts. Osteoblasts are responsible for bone formation, whereas, osteoclasts are responsible for bone resorption. Both are very important in maintaining healthy bone tissue. Disturbance in the number of osteoblasts and osteoclasts can lead to bone loss, which can further lead to a disease called osteoporosis. Pyk2 is a tyrosine kinase that also has an effect on the density of bone. Previous studies in our lab have shown that deletion of Pyk2 in mice leads to an increase in bone mass. Pyk2 phosphorylation is shown to be important for its catalytic activity. On the other hand, Kalirin is a GTP exchange factor protein that is also linked to bone mass, and deletion of Kalirin in mice results in a low bone mass. Kalirin is expressed as different isoforms, each of which contain different functional domains. To determine if Kalirin plays a role in Pyk2 phosphorylation, Kalirin domains will be expressed with or without Pyk2 in MC3T3-E1 cells and HEK293 cells by transient transfection. After 3 days, the cells will be lysed and proteins will be resolved on SDS-PAGE gels. Western blotting will be performed using an antibody to phosphorylated Pyk2-Y402 or with an antibody that detects the Kalirin domains. These results will help understand the relationship between Kalirin and Pyk2 phosphorylation in regulating osteoblast function.

Environmental Barriers and the Impact on Executive Functioning Challenges on Community Mobility for Individuals with Acquired Cognitive Disabilities

The purpose of this study is to better understand the environmental barriers and every day challenges that individuals with acquired cognitive disabilities (ACD) and their caregivers face while getting around in the community. Using a semi structured interview approach, derived from a phenomenological perspective, we asked the participants open ended questions about the barriers and challenges they face when moving about the community. At this point in the study we have too few interviews to have reached saturation in the participants’ responses. Based on only seven interviews transcribed and analyzed so far, the participants seem to primarily rely on family or friends, on the paratransit system, or other private transportation systems such as taxis to get around in the community. Among the finding so far, the challenges of scheduling trips to assure getting to medical appointments stands out. Participants often missed medical appointments or were isolated in their homes for lack of reliable transportation. Even with the research still under way the researchers anticipate findings that demonstrate that individuals with acquired cognitive disability and their caregivers experience significant challenges to community mobility due to cognitive challenges and physical environmental challenges resulting from ACD. This study supports the need for health care providers to have a better understanding of what environmental barriers and everyday challenges patients with ACD and their caregivers might experience with community mobility. Furthermore, it supports the need for discharge planning that includes identification of patients’ community mobility needs that includes offering patients information about available community mobility resources.
Neurotelemetry with Trending and Quantitative Analyses Evaluates Outcomes in Patients Undergoing Therapeutic Hypothermia Following Cardiac Arrest: Preliminary Results

Introduction: Over 160,000 cardiac arrests occur outside of hospitals in the US each year with over 80% of those resuscitated remaining comatose in the initial post-resuscitation period. Studies have shown improved outcomes for these patients if they are treated with mild, therapeutic hypothermia in the immediate post arrest period, but significant challenges remain in the treatment and prognosis of these patients. The use of intermittent EEG recordings has been studied, but this method can miss seizure activity making the utility of the non-continuous recordings unreliable. Real-time, continuous EEG monitoring with video (Neurotelemetry) accommodates for this shortcoming and is currently offered at Methodist Hospital.

Purpose: A pilot study is being conducted to develop outcome predictors and demonstrate improved outcomes using Neurotelemetry with trending and quantitative analyses to aid clinicians in the care of these patients. Preliminary results: EEG data from a sample of 33 patients was analyzed. Values from channels FP3 and FP4 were used to determine the average alpha variability (AV) and alpha/delta ratio (ADR). These values were compared between patients who survived through hospital discharge and those who died prior to discharge. It can be seen that patients with a lower average AV and ADR on days 3, 4, 5 tend to have a more positive outcome and increased odds of recovery. Conclusion: Based on preliminary findings, patients that had a spike in average AV and ADR on day 2, followed by a decrease in average AV/ADR for the next following 3 days, while under induced-hypothermia, tend to have a better chance of survival compared to the average AV/ADR of the deceased patients. This displays that average AV/ADR can be used as a potential indicator of patient outcome.

Role of Dynamin in Regulating Osteocyte Dendrite Elongation

Osteocytes are bone cells that are located within the mineralized bone matrix. They are known to orchestrate bone remodeling by regulating the activity of both osteoblasts (bone-forming cells) and osteoclasts (bone-resorbing cells). Osteocytes contain membrane extensions known as dendrites, which allow cell-to-cell coupling with other osteocytes, osteoblasts, and osteoclasts. However, the mechanism for dendrite formation is still uncertain. In this project, we investigate the role of Dynamin in regulating osteocyte dendritic elongation. Dynamin is an enzyme that hydrolyzes GTP to GDP and is involved in various cellular activities, such as clathrin-mediated endocytosis and actin remodeling. Previously, we demonstrated that Dynamin is crucial for regulating osteoblast migration and differentiation as well as bone resorbing activity by osteoclasts. To understand the role of Dynamin in osteocyte dendrite formation, MLO-Y4 osteocytic cells were treated with various concentrations of dynasore, a chemical inhibitor of Dynamin for 1-3 days. The cells were imaged each day using a Leica DMI 4000B microscope. The lengths of dendrites were measured using ImagePro software. In addition, lysates from dynasore-treated and untreated control cells were used for Western blot analyses. Statistical significance was determined using student t-Test (p<0.05). Our results showed that the dynasore-treated cells exhibited a significant (150%) increase in dendrite length, which occurred in time-dependent manner. Furthermore, there was a significant increase in protein expression of Vav and PTP-1B, which are important for remodeling of the actin cytoskeleton. Overall, our results suggest that Dynamin may play a critical role in bone remodeling by regulating dendrite elongation in osteocytes.
Streptococcus mutans Binding to Collagen and Fibrinogen in Nicotine

Introduction: Atherosclerosis is a complex disease that is caused by arteries hardening due to a build up of plaque. There is a possibility that it is related to dentistry. Patients who smoke have more Streptococcus mutans in their mouths and because of this may have an increased risk of atherosclerosis. The main goal of this research is to find the mechanism of atherosclerosis, so that the biological causes can be known.

Objective: The objective of this study was to assess the binding of S. mutans to fibrinogen and collagen type I. These proteins naturally appear on the surfaces of endothelial cells that line the arteries.

Methods: Methods included culturing S. mutans in varying nicotine concentrations, biotinylating the bacteria cells, plating the proteins, blocking the empty gaps with BSA, plating the bacteria, and staining and analysis of the bacteria. The intensity of absorbance was directly related to the number of S. mutans bound to the protein.

Conclusion: In 2 and 4 mg/mL dilutions, binding was the highest. The data collected indicates that protein binding increases when S. mutans are cultured in tolerable concentrations of nicotine.

Predictors in Driving Restrictions: Vision Testing

In 2006, there were approximately more than 30 million people that were licensed drivers 65 years or older. By 2030, the elderly population could be increased to 72 million people. They all can pose risks in their own way. Vision is a key factor in driving. For people ages 75 and older, they had the following percentage of problems related to them for vision and driving, women 84% and men 75%. Vision problems that affect driving are macular degeneration, diabetic retinopathy, glaucoma, and hemianopia. Participants in driving assessments could be tested for color identification, visual acuity, depth perception, vertical and lateral phoria, road sign recognition, and field of vision. Contrast sensitivity and Useful Field of View can also be tested and can show great predictors in driving restrictions. Any of these visual deficits and decreased levels in tests can lead to an increased risk of car crashes. The goal of this study was to find vision variables that could predict driving restrictions or problems with older drivers. It investigated what types of tests can be done to show these results and what can be done to restrict dangerous visual impaired drivers. The Global Rating Scale has determined the different ratings each visual impaired driver might result in. The scores range from zero to three, zero being all restrictions, and three being no restrictions. The results from all of these different driving assessments can determine what changes need to be made to the driver to keep themselves and other drivers safe.
Transthyretin Amyloid Cardiomyopathy

Transthyretin Amyloid is a rare genetic disease caused by mutations in transthyretin (TTR). TTR is a plasma protein synthesized primarily by the liver. Mutations in TTR lead to peptide aggregation and formation of insoluble fibril deposits (amyloid). The main outcomes of TTR amyloidosis are progressive peripheral and autonomic neuropathy and restrictive cardiomyopathy. Amyloidosis is a familial disease that travels from generation to generation. There are one hundred and fourteen different variations of Amyloidosis. This study’s primary objective is to determine the safety and tolerability of the given drug over a twenty-four-month period, and how it effects the production of TTR. The patients take a single injection once a week as a part of regulation and safety. The study looks for baseline changes in multiple tests such as: echocardiogram (ECHO), modified body mass index (mBMI), TTR, BNP, 6 minute walk, NYHA score, and the cardiac magnetic resonance imaging (MRI). Each respective test measures how the patient’s heart is dealing with the progression of the disease, and how the study drug is affecting the heart. The TTR value is critical to the overall study. The study drug is focused on human TTR mRNA and its hybridization to the cognate TTR mRNA results in the RNase H-mediated degradation of the TTR mRNA, thus preventing production of the TTR protein. It is predicted that reducing the amount of liver-derived TTR protein in the plasma by treatment of the study drug will result in a decline in the formation of TTR amyloid fibril deposits, and thus slow or halt the disease. This is an ongoing study; therefore definitive results are not available.

Probing Adrenoceptor Modulators as Relaxants for the Mouse Uterus.

Preterm birth remains the leading cause of neonatal morbidity and mortality in the United States and around the world. Nonetheless, little is known about the actual mechanisms behind the cause of preterm labor. In an attempt to answer this mystery, we investigated the effects of adrenergic receptor agonists on contractility of mouse uterine smooth muscle using an isometric tension measurement approach. Adrenoceptors are subdivided into alpha and beta receptor subtypes that are activated by norepinephrine and epinephrine. In this study, we focused on the beta receptor agonists. During the initial experiments, smooth uterine muscles of non-pregnant mice were used. We identified adrenoceptor agonists that exhibit a potent relaxing action on the uterus of non-pregnant mice. Such agonists may serve as the lead compounds for drug development teams working on establishing novel treatments for preventing preterm labor.
Intern: Kyle McElyea  
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Mentor: George Sandusky  
Department: Pathology

Quantitative Immunohistochemistry Evaluating APE1 Expression in a Mouse Pancreatic Adenocarcinoma Model

High levels of APE1 expression have been reported in numerous cancers (glioblastoma, ovarian, pancreatic, prostate, and others) such that APE1 is an emerging target for a variety of novel anticancer drugs. Human apurinic endonuclease/redox factor 1 (APE1/Ref-1) mediates the repair of baseless sites in DNA caused by alkylation and oxidative DNA damage. E3330 targets the redox signaling function of APE1 and its activity was studied in vivo using a pancreatic adenocarcinoma xenograft mouse model. This preclinical xenograft model evaluated the use of anti-angiogenic and anti-proliferative agents, Gemcitabine and E3330, in pancreatic adenocarcinoma implanted NSG (NOD) mice. In this study, eight mice groups were used to determine drug effects of: E3330 (12.5mg/kg, 25mg/kg, and 50mg/kg), Gemcitabine (35mg/kg), a combination of E3330 and Gemcitabine (12.5mg/kg, 25mg/kg, and 50mg/kg), and an untreated vehicle control group. At termination of the study, tumors were harvested and cross-sections were processed into a Paraffin block. Tissue sections were prepared and stained for H&E and immunostain for CD31 (angiogenesis marker). The immunostains were evaluated to predict the effectiveness of treatment for pancreatic adenocarcinoma. IHC slides were quantitated using an Aperio positive pixel algorithm to determine the percent of angiogenesis in the various drug treatment groups. A biologically significant correlation was seen amongst the low and middle dose E3330 drug groups. These groups had anti-angiogenic effects that were slightly lower than a combination of E3330 and Gemcitabine at the same dose treatment groups. These results support previous studies demonstrating the anti-angiogenic activity of E3330.

Intern: Seth McKinney  
Major: Biology  
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Induction of NADPH Oxidase Subunits in Post-Ischemic Rats Fed on High Salt Diet

Acute kidney injury (AKI) due to renal ischemia or sepsis represents a major clinical problem associated with significant mortality. Sustained renal oxidant stress following recovery from AKI alters both renal hemodynamic and immune function, which contributes to the transition to chronic kidney disease following AKI. Previous studies involving anti-oxidants suggest that the early rise in ROS contributes to tissue damage and the loss of renal function post AKI. Surprisingly we did not measure an insignificant change in induction of NADPH oxidase subunits in whole kidney tissue (1). In another study, an increase in p67phox subunit of NADPH oxidase was measured in infiltrating renal T-cells in hypertensive rats (2). As our studies indicate that T cells specifically Th17 cells are associated with AKI to CKD progression, we hypothesized that an increase in oxidative stress measured post-kidney injury may be due an increase in NADPH oxidase activity in infiltrating T-cells post-kidney injury. AKI was induced by unilateral I/R rats were subsequently put on low salt diet (0.4 NaCl.) After 5 weeks of recovery, unilateral nephrectomy was performed and the rats were placed on high salt diet (4.0% NaCl) to hasten chronic kidney disease. Kidney was harvested and T cells were isolated. Quantitative RT-PCR analysis was performed to compare expression in whole kidney cells vs. isolated T-cells. As similar mRNA levels of gp91 and p22 in whole kidney cells and isolated renal T cells was measured from sham and injured kidney, hence we suggest that in our model system infiltrating T cells are not associated with ROS generation.
Intern: Mackenzie McLean
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Mentor: Sharon Cromer
Department: Clinical Research Center

Analysis of the essential steps taken by the CRC in proving adequate patient support

The Indiana Clinical Translational Sciences Institute (CTSI) is a statewide collaboration of Indiana University, Purdue University, and the University of Notre Dame. The CTSI also includes public and private partnerships, which facilitates the translation of scientific discoveries in the lab into clinical trials and new patient treatments. The National Institutes of Health continues to support the CTSI to create an environment that brings together the resources of academic, commercial, and community groups across the state. The mission of the Indiana CTSI is to increase translational biomedical research and improve the health of people of Indiana and beyond. This mission is greatly facilitated by the Indiana CTSI Clinical Research Center (CRC) at IUPUI, as a major resource at Indiana University School of Medicine for performing quality clinical research. The CRC provides inpatient and outpatient resources, as well as nursing and nutrition support. They conduct both adult and pediatric study protocols in various disciplines including: diabetes, gastroenterology, neurology, oncology, gynecology, rheumatology, psychology, and psychiatry. In order for the CRC to continue running smoothly each day, it is important for the administration, nursing, nutritionist, and study coordinators to work together in maintaining adequate patient support. The purpose of the project is to provide a patient support flow chart and analysis of the essential steps taken by each CRC staff member to ensure the patient or study participant receive adequate care throughout their visit.

Intern: Susan Mertz
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Prominent Negative Emotionality in Youth at High Risk for the Development of Substance Use Disorders

Substance use disorders (SUDs) are one of the most harmful preventable health conditions in society today. Many factors contribute to the development of an SUD including genetic predisposition and environmental aspects. Most addictions liability models implicate emotion regulation constructs such as irritability, negative affectivity, and distress intolerance as possible characteristics in the development of an SUD. This study separates children between the ages of 10-14 years into high risk and low risk groups for the development of SUDs. Children in the high risk group have externalizing disorders and are the offspring of men with SUDs. Low risk participants are typically developing children without a first degree relation with an SUD. This research project examined the severity of positive and negative emotionality in both high and low risk populations using the Differential Emotions Scale (DES-IV), a well-established 36-item questionnaire that is used to dissect components of negative affectivity. An analysis of covariance, accounting for group differences in IQ and socioeconomic status, compared the groups’ DES-IV total and subscales. We report between group differences in 7/9 negative emotional subscales. These results suggest that emotions such as fear, guilt, and contempt may play an important role in the development of SUDs.
Intern: Stephanie Michalski  
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Mentor: Jinhui Chen  
Department: Neurological Surgery  

TBI Severity Affects Neural Stem Cell Proliferation in the Adult Hippocampus.

Currently, traumatic brain injuries (TBI) are the primary cause of death within both children and young adults. Following TBI, cognitive impairment such as learning and memory deficits are of high concern due to the lack of effective treatment options in society today. Discovery of neural stem cells (NSC) in the adult mammalian brain provides a promising outlook to the future for possible therapeutic treatment for TBI. Exploring the molecular process of neurogenesis post TBI may lead to the development of approaches that enhance successful neurogenesis, thereby repairing the cognitive deficits characteristic of TBI and enhancing learning and memory. Currently, little information is known concerning how various levels of TBI severity impact neurogenesis post injury. Our preliminary data suggested that moderate TBI significantly promotes NSC proliferation. The aim of this project is to determine the effects of TBI severity on the proliferation of NSCs. TBI was conducted via a controlled cortical impact model. BrdU is used as a marker to trace the fate of NSCs following TBI. Sox2 is a critical transcription factor controlling NSC self-renewal, and is therefore used as a NSC marker. BrdU and Sox2 double-positive cells in the SGZ represent NSC proliferation. Our results indicate that mild TBI does not affect NSC proliferation, while moderate TBI promotes NSC proliferation and severe TBI significantly increases NSC proliferation in the SGZ of the HDG. This strongly indicates that TBI promotes NSC proliferation in the hippocampus and the promotion of NSC proliferation is directly correlated to the level of TBI severity.

Intern: Casey Miller  
Major: Biology  
Mentor: Maria Grant, Lynn Shaw  
Department: Ophthalmology  

TLR Pathway Involvement in Diabetic Retinopathy

Toll-Like receptors (TLRs) are key molecular regulators of inflammation, expressed in leukocytes and in endothelial cells. TLR4 gene polymorphism was previously shown to be one of the genetic factors influencing propensity of diabetic retinopathy (DR), and its manipulation in animal models of DR could largely reduce the leukocyte-induced vascular damage. However, less is known about TLRs role in more primitive circulating cells, such as the CD34+ bone marrow derived cells, that are important contributors to the progression of diabetes-induced pathological neovascularization in the eye. In this study, CD34+ cells from diabetic patients with DR and from a group resistant to DR, as well as from control subjects, were analyzed for gene expression by Affymetrix microarrays and then TLR-2, -3, -4, and -8, and IL1b were further validated by real-time PCR. We found that in patients resistant to DR, TLR-4 and -8 were significantly lower as compared to those that develop the disease and closer to the non-diabetic controls. TLR-2 expression was increased in all diabetic patients, while TLR-3 expression was very low in all samples. IL1b was significantly increased in diabetic patients, however less so in those protected of DR. In conclusion, a reduced activation of inflammatory pathways in circulating CD34+ cells seems to provide protection against the development of DR, a finding which can be exploited for both diagnostic and therapeutic purposes.
Characterization of Family Functioning in Youth at Elevated Risk for Substance Use Disorders

The Neural Correlates of Emotion Dysregulation in Youth at Risk for Substance Abuse/NIDA study was conducted as a pilot for a longitudinal analysis, to provide insight on the role of atypical emotional processing in the development of substance use disorders. In this study, participants were placed into two groups, (High Risk and Low Risk), based upon risk status for substance abuse disorders (SUDs). Participants were males and females 10-14 yrs. of age (n = 61, 62.3% male, 37.7% female, 41% Caucasian, 41% African American, 14.8% Biracial, 3.2% Other). Here we present group comparisons of the Family Assessment Measurement (FAM) to examine the significance of family strengths and weaknesses. Parental guardians and participants each filled out FAM III Self-Rating Scales. Univariate Analysis of Variance was used to examine a main effect of group for both the parental overall scores (F= 19.16, p<.001) and child overall scores (F= 22.45, p< .001) when accounting for covariates of both income of the parent and IQ of the child. Findings suggest that youth and parents in families at high risk for youth SUDs perceive their family functioning to be highly dysfunctional. Future studies following up this sample will be able to address the impact of impaired family functioning on the development of SUDs.

Gene interaction of TGFbeta2 with SOXC is critical for normal heart development

Congenital heart disease (CHD) is an important component of pediatric and adult heart disease and constitutes a major portion of clinically significant birth defects. The etiology of cardiac malformations largely remains unknown. An incidence of pediatric heart disease of 50 per 1,000 (5%) live births is a conservative estimate. Consequently, CHD constitutes an important medical issue. Heterozygous loss of function mutations in TGFbeta2 is found in patients of Loeys-Dietz Syndrome (LDS). Significant portion of LDS exhibit some form of congenital heart disease (CHD) (i.e., ventricular septal defects, bicuspid aortic valve etc.); however, heterozygous loss of Tgf2 (Tgf2+/-) alone is insufficient to cause CHD in mice, as majority of all people with TGFbeta2 heterozygous mutations have a normal heart, suggesting that genetic modifiers within or outside of the TGFbeta2 pathway interact with TGFbeta2 in dosage-sensitive manner to result in CHD. The variable occurrence of CHD in the patients and lack of CHD in the Tgf2+/- mice (genetic model) have made the identification of molecular mechanisms and function of TGFbeta2 in CHD extremely challenging. We speculate that a threshold exists in LDS population for a number of genetic perturbations within the TGFbeta pathway that can be tolerated before CHD results. Our hypothesis is that Tgf2+/- mice represent a sensitized or susceptible mouse model much closer to the threshold for fully penetrant CHD and therefore offer a unique opportunity to uncover downstream molecular signaling pathways of TGFbeta2. Based on the similar gene expression patterns of Tgf2 and SoxC in the developing heart, we initiated studies to determine if interaction of Tgf2 with SoxC is required for heart development. SOX4, SOX11, and SOX12 are collectively referred to as SOXC. SOXC proteins are transcription factors which act in cell-autonomous fashion.
Identification of a resilient population of axotomized motoneurons within the mouse facial motor nucleus

Previous facial motoneuron (MN) survival studies have identified a facial MN population that is resilient to axotomy. Examination of the literature suggests two distinct populations of MN: one population vulnerable to axotomy and another population potentially resilient to axotomy. To identify potential differences in MN survival levels after target disconnection, we performed a facial nerve transection at the stylomastoid foramen in a number of different mouse strains, as well as models of immunodeficiency and MN disease. All mice were monitored for facial MN survival for up to 26 weeks post-axotomy (wpa). We observed an 85% survival of facial MN at 4 wpa that was reduced to about 50% at 10 wpa in WT mice. In contrast, facial MN survival significantly dropped at 4 wpa to approximately 62% and 50% in immunodeficient and MN disease mice, respectively. Similar to WT mice, facial MN survival levels remained at about 50% for up to 18 wpa in both the immunodeficient and MN disease mice. Collectively, these data suggest that, despite target disconnection of similar MN populations by either axotomy or disease, there are inherent differences that may be exploited for therapeutic applications in the future.

Factors affecting SIRT6 gene expression

SIRT6 is a regulatory protein found in the nucleus of every cell whose expression can modulate DNA repair, glucose metabolism, cancer, telomere maintenance, lipid metabolism, inflammation, stress, and heart function [1]. However, the complete set of sequence-specific transcription factors that regulate the sirtuin 6 gene SIRT6 are not well characterized. In this experiment, an attempt was made to build a high resolution map of its transcriptional regulation. In silico phylogenetic footprinting was conducted on the upstream regulatory regions of a diverse set of human SIRT6 orthologues to identify conserved binding motifs and corresponding position-specific weight matrices. We further analyzed the predicted binding motifs by motif comparison, which identified transcription factors likely to bind these discovered motifs [2]. Predicted transcription factors were then integrated with experimentally known protein-protein interactions available from public databases and tissue-specific expression resources to delineate important regulators controlling SIRT6 expression [3]. Analysis allowed the identification of a reliable set of binding motifs in the upstream regulatory regions of SIRT6 to build a set of predicted transcription factors that could bind these motifs, such as GAPBA, E2F4, and Sp1. ENCODE deoxyribonuclease I hypersensitivity sites in the SIRT6 upstream region confirmed that some of these binding motifs were open to binding by predicted transcription factors. The findings may help form a map for understanding the regulation of SIRT6 expression in health and disease.
Intern: Paxton Ott  
Major: Exercise Science  
Mentor: Jingyun Wang  
Department: Ophthalmology  

Compliance with AmblyzTM Liquid Crystal Glasses Versus Traditional Adhesive Patches

PURPOSE: Amblyopia treatment with adhesive occlusion patches is frequently inhibited by poor compliance and complaints. Amblyz™ liquid crystal glasses utilize a 50% intermittent occlusion technique (at 30-second opaque/transparent intervals) and avoid adhesives, potentially improving compliance. This study compares compliance with AmblyzTM glasses versus patching.  
METHODS: Children (N=28, age=5.3±1.4YR, 3- to 8-year-old) with previously untreated, moderate, unilateral amblyopia (visual acuity of 20/40 to 20/100 in the amblyopic eye) were enrolled. All subjects were optimal refractive correction for at least 12 weeks and their amblyopia was associated with strabismus, anisometropia, or both. Subjects were randomized into one of two treatment groups: a 4-hour Amblyz™ Glasses Group, or a 2-hour Patching Control Group. After 12 weeks, compliance was reported with a calendar log and an Amblyopia Treatment Index (ATI) questionnaire characterizing the experience.  
RESULTS: At the conclusion of the first 12 week-treatment interval, compliance averaged 93% in the Patching Group and 79% in the AmblyzTM Group. Weekly compliance varied among individuals. The ATI questionnaire demonstrated a high level of enthusiasm from parents and children with the Amblyz™ glasses, commonly remarking that they were easy to wear and generated few complaints.  
DISCUSSION: These preliminary results are limited by the small sample size and short-term follow-up.  
CONCLUSION: Compliance with AmblyzTM glasses is similar to patching, even when wearing time was doubled in this trial. This device is a promising alternative to the traditional patching amblyopia treatment that promotes a relatively comfortable experience for the child.
Intern: Emily Parker  
Major: Biology, Neuroscience

Mentor: Leslie Hulvershorn  
Department: Child Psychiatry

Callous and Unemotional Traits in Youth at Low and High Risk for Substance Use Disorder Disorders

Adolescents who report callous unemotional (CU) traits are shown to be at an increased likelihood of substance use and impairment onset and recurrence. The existence of CU traits prior to a SUD may open a new door in the treatment of SUD through increasing prevention measures in high-risk individuals. The purpose of this study is to verify whether callous or unemotional traits differ significantly between 10-14 year olds at high and low risk for SUDs (n=61). All subjects completed the Inventory of Callous Unemotional (ICU) traits. ANCOVA was used to compare groups on subscales of the ICU. Results demonstrate that, when controlling for IQ and socioeconomic differences, high risk adolescents have a significantly higher degree of callous (P=0.037, F=4.552) and uncaring (P=0.007, F=7.843) traits than low risk adolescents. With future longitudinal follow-up, CU traits may be a target for SUD prevention in high-risk adolescents.

Intern: Niral Patel  
Major: Kinesiology

Mentor: Jennifer Taylor  
Department: Family Medicine

Primary Care Physician Job Satisfaction

The primary objective of this study was to identify the different factors that go into physician job satisfaction and develop potential strategies to improve primary care retention among physicians in primary care settings across Indiana in hopes of closing the gap between physicians and patients. To identify these factors, family medicine physicians will complete a survey measuring influencing factors and personal thoughts on occurrences in the primary care field. Throughout the progression of this qualitative study, many unforeseen complications and errors occurred, leading to an incompleteness of the project. The lessons learned from errors and complications during this research experience provided deep insights into the process of research. Though the study was unsuccessful, the project resulted in a substantial learning experience.
Parental Support and Communication About Sex Topics

Sexual initiation has been positively associated with parent-adolescent communication about sexual health topics. The present study aims to investigate the relationship between sexual risk behaviors, parental support, and family communication about sexual health topics. Data for this analysis comes from the Youth Personal Responsibly Education Program (Y-PREP) study, a longitudinal study designed to understanding how a mother’s relationship with her child influences the child’s risk and protective behaviors, attitudes, and experiences and opinions of a sex education curriculum. Due to the ongoing nature of the study, the following findings are from the baseline dataset and can therefore be considered cross-sectional. Out of 100 adolescents 43 who were younger than 14 were not asked about sexual behaviors. Adolescents who reported having had vaginal intercourse were more likely to have talked to their mothers about sexual health topics than those who did not (p=.006). In addition, adolescents who reported not having used a condom during last intercourse were also more likely to have talked to their mothers about sexual health topics than those who reported otherwise (p=.035). Perceived parental support was also assessed. In general adolescents who perceived a lower level of parental support from their mothers reported a higher number of oral sex partners in their lifetime (r=.300, n=51, p=.033) and in the past six months (r=.282, n=51, p=.045). These findings highlight the need to explore the quality of mother-adolescent communication about sexual health topics and the potential to address parental support and communication with parents in sexual education curricula.

Effects of Nicotine on Aerobic and Anaerobic Serotype K Streptococcus mutans Biofilm Formation

Atherosclerosis is a specific form of arteriosclerosis where the walls of arteries began to thicken as a result of bacterial invasion and accumulation of inflammatory white blood cells. There could be a direct correlation of atherosclerosis and the intake of nicotine. Nicotine has been reported to increase the amount of the cariogenic oral bacteria known as Streptococcus mutans; thus possibly leading to an increase of dental caries. Serotype K S. mutans has been associated strongly with atherosclerosis. Objective: This study focused on the biofilm formation of S. mutans serotype K when incubated in dilutions of nicotine. Methods: S. mutans UA159 (stereotype C), and stereotype K strains 89, 52, and 51 were cultured in tryptic soy broth (TSB) overnight and then added to dilutions of TSB with 1% sucrose (TSBS) containing concentrations of nicotine between 0 and 32 mg/ml. Each dilution was added to 96-well microtiter plates, inoculated with bacteria, and incubated for 24 hours aerobically and anaerobically. The plates were treated with formaldehyde, crystal violet, and isopropanol and biofilm formation was measured. Results: Strains UA159, 89, 52, and 51 all demonstrated significantly higher biofilm formation (p<0.05) at a nicotine dilution of 8 mg/ml. When comparing the anaerobic results to the aerobic results, anaerobic incubation increased the overall biofilm formation across the majority of nicotine dilutions. Conclusion: It was established that when S. mutans strains UA159, 89, 52, and 51 were incubated anaerobically and aerobically biofilm formation was enhanced which may lead to increased binding to endothelial cells contributing to atherosclerosis.
Intern: Kayla Quirin  
Major: Psychology  
Mentor: Hiromi Tanaka  
Department: Medical and Molecular Genetics  

Understanding the relationship between telomerase activity, telomere length, and cancer

Capping the end of each chromosome in the body are telomeres, a highly repetitive region of DNA. In normal cells, telomeres shorten with each replication cycle due to the end replication problem. Telomeres hit a point of critical shortening and lose protective caps, leading to telomere fusions and genomic instability. Cancer cells have particularly stable telomeres because they express telomerase which adds TTAGGG repeats to the telomere. Telomerase is re-activated or up-regulated in more than 90% of cancerous cells, allowing them to continue proliferation without degradation of telomeres. This means that telomerase activation is required for the unlimited proliferation of almost all cancer cells. To better understand the relationship between telomeres, telomerase, and cancer and to potentially find a way to use that relationship in earlier cancer detection, two projects were conducted. In the first project, we hypothesized that telomere length is controlled by the activity of telomerase in cancer cells. To test this, telomere length and telomerase activity were measured in various cancer cell lines to determine a relationship. In the second project, the focus was the potential utility of using telomerase activity in plasma for cancer diagnosis. This required a comparison of plasma telomerase activity in cancer patients versus non-cancer patients. Both projects used TRAP (Telomere Repeat Amplification Protocol) assay to measure telomerase activity and Southern Blot to measure mean telomere length. Preliminary results indicate a trend that the level of plasma telomerase activity may potentially help determine breast cancer.

Intern: Kaitlin Reeves  
Major: Biology  
Mentor: Robert Orr  
Department: Clinical and Translational Sciences Institute  

Clinical and Translational Support Laboratory

The CTSL provides various services to its partners, including: set-up, sample preparation, benchwork, and post-processing services. During set-up, kits for various studies are prepared by labeling all test tubes and aliquots according to protocol specifications. Benchwork involves following each protocol’s requirements; this often involves specific centrifuge temperatures, clotting times, and centrifuge speeds. Often, this involves separating various components of each sample, such as plasma, clots, or white blood cells. Post-processing services vary across protocols. The CTSL stores samples in various freezers or refrigerators, according to each sample’s specifications. Study information, including patient information, storage location, number of aliquots collected, and collection times, is recorded for many protocols in an online database. The CTSL also offers a shipping service for the processed samples. These services are imperative to the progress of the their partners’ research due to its help in saving the researcher’s time and effort while following a strict schedule of regular equipment maintenance and a system of checks and balances within the CTSL. From its start, the CTSL has grown, both in its number of partners and the services it has provided, such as the relatively new shipping service. CTSL benefits its partners by lessening the labor and time they must spend processing their samples, while also providing detailed and important maintenance and quality assurance on every sample.
The Effects of 17β-Estradiol on Proliferation in Pulmonary Vessels in Rats with a Severe Angioproliferative Model of Pulmonary Hypertension

Pulmonary Hypertension (PH) is a progressive cardiopulmonary disease characterized by the formation of plexiform lesions and an increase in proliferation of smooth muscle (SMC) and endothelial (EC) cells within small pulmonary arteries. As a result, pulmonary arterial pressure increases (>25 mm Hg) which ultimately leads to right ventricular failure and death. Research has shown that the ratio of males to females affected by PH is approximately 1:2, yet females have a higher survival rate after diagnosis. This data suggests that estrogen plays a crucial role in the pathogenesis and development of PH, however its effect on SMC and EC, which makes up the pulmonary arteries, is not yet known. To better understand the role of estrogen in the Sugen Hypoxia (SuHx) Model of PH, rat lung tissue was stained and analyzed to identify the number of proliferating cells. Cells were counted positive for proliferating cell nuclear antigen (PCNA), a marker for cells in S-phase, and co-localized to the SMC and EC cell layer. In this study, normoxic females were found to have higher amounts of PCNA in ECs than normoxic males. Additionally, it was found that ovariectomized (SuHx OVX) female rats tended to have an increase in total SMC and EC proliferation but had a decrease in total proliferation after they were replenished with 17β-Estradiol (SuHx OVX+E2). In conclusion, we found sex differences in proliferative responses in the pulmonary vasculature of control rats that increased in a model of PH and was attenuated by E2.

Nanobody-aided X-ray Crystallography of the Mediator Head Module

Mediator is a large multi-protein complex that regulates transcription by RNA polymerase II (Pol II). Therefore, understanding molecular mechanism of the Mediator function is essential in biomedical sciences. Mediator is composed of a total of 21 subunits, and organized into three modules termed Head, Middle, and Tail. The Takagi’s laboratory determined the structure of the Mediator Head module by X-ray crystallography at 4.3 angstrom resolution. However, its conformational flexibility has compromised rigidifying the complex essential for obtaining highly diffracting crystals for high-resolution structure determination thus far. To circumvent this problem, we collaborated with Steyaert’s laboratory, and generated the nanobodies (Nbs) - engineered single viable domain derived from antibodies from llama- which could be used rigidify the Head module for high-resolution structure determination. Previously, 8 Nbs were selected out of 90 Nbs using Thermo-fluor method. The 8 chosen Nbs were prepared in large quantities for crystallization trials for the Head-Nb complex. The 4 (Nb1, Nb2, Nb3, Nb4) out of 8 Nbs were mixed individually with the Head module and subjected to crystallization trials using Wizard 1, 2 and 3 screening kits. The 14 crystals emerged in a wide array of crystallization conditions. Several optimizations were followed, which led to identify the condition in which the Head-Nb3 yielded large crystals. Future plan includes further optimization of the condition using additive screens, and testing the X-ray diffraction of the crystals, aiming toward generation of the Head-nanobody crystals that extend their diffraction limit, enabling to determine the structure of the Mediator Head module at atomic resolution by X-ray crystallography.
Saliva Processing and Periodontitis

Periodontitis is a serious gum infection that damages the soft tissue and destroys the bone that supports your teeth. It causes tooth loss or an increased risk of heart attack or stroke and other serious health problems. Periodontitis is initiated by a broad array of bacteria and is perpetuated by an immune inflammatory response to the changing biofilm. Recognition of tons of bacteria are mediated by toll-like receptors (TLRs), which interact with conserved pathogen-associated molecular patterns. TLR-2, pro-inflammatory cytokines, and TLR-4, anti-inflammatory cytokines, interact with most periodontal pathogens. The objective of this study was to investigate the response of oral epithelial cells to concurrent exposure to two common periodontopathic bacteria, Fusobacterium nucleatum (Fn) and P. gingivalis (Pg). To recognize how TLR's bind and respond by releasing cytokines. Our study consisted of human saliva that was collected from patients with periodontitis and healthy individuals with informed consent from IUPUI. Human saliva is a rich source of oral epithelial cells that express functional TLRs. The epithelial cells from unstimulated whole saliva was isolated and stimulated for a couple hours with different ratios of the periodontal pathogens F. nucleatum and P. gingivalis. The levels of IL-8 and IL-12 were measured using enzyme-linked immunosorbent assay (ELISA). Results indicated that in order to reduce levels of IL-8 from P. gingivalis bacterium, there must be a balance between F. nucleatum and P. gingivalis. Overall, periodontitis cells responded differently than normal cells to bacterial treatment.

Influence of Bone Morphology on Raloxifene-mediated Improvements in Bone Mechanics

Raloxifene is an FDA approved agent used to decrease the likelihood of bone fracture. Raloxifene improves the mechanical properties of bone independent of altering the bone mass, but its mechanisms are unclear. The goal of this work is to determine if Raloxifene has a differential effect on the mechanical properties, specifically bone toughness, in bones that have different morphologies. Robust bones, defined as having a large total cross-sectional area divided by total length, are known to have higher bone toughness compared to slender bones (those with low area/length ratio). Therefore, our hypothesis was that raloxifene would improve toughness in slender, but not robust bones. To test this hypothesis, bones from robust and slender dogs, mice, and human donors were cut into beams. The beams were then exposed to Raloxifene for two weeks before being mechanically tested using 4-point bending. Our data showed evidence that, after soaking for two weeks in Raloxifene, highly robust canine bones are relatively unaffected while slender canine bones had significantly higher toughness. When this experiment was repeated in mice and humans, the overall average in Raloxifene-soaked slender bones showed greater toughness compared to robust bone, yet the results were highly variable among individuals. These findings suggest that morphology may influence how raloxifene affects bone mechanical properties yet there appear be other factors that exist within each morphology classification that interact with drug exposure.
Intern: Craig Schebler  
Major: Computer Science  
Mentor: Ashay Bhatwadekar  
Department: Ophthalmology  

Computer-based quantification of acellular capillaries to assess experimental diabetic retinopathy

Purpose: Increase in acellular capillary numbers is the pathologic hallmark of diabetic retinopathy. The purpose of this study is to create a computer-based algorithm that will assess the acellular capillaries of the retina, consistently reducing the human error and time. Methods: The retinas of control and diabetic mice were processed using trypsin digestion and the high resolution .tiff images of retinal quadrants. The images underwent a Gaussian blur and noise reduction to clean up the imperfections of the image. We used a purpose-built k-means clustering algorithm to group similar parts of the image together. We generated the paths in each image by converting all non-white elements to black. These images were then processed for Medial Access Transform (MAT) to create the skeleton as well as to find the distance from the skeleton to the edges formed in the above steps. The colors represent the distance from the edges, in which red is the largest distance and purple is the shortest distance. Then the locations where the distance was minimal are counted as acellular capillaries. Results: We have developed a precise algorithm with improved accuracy to enumerate the numbers of acellular capillaries. This algorithm can be used to quickly count the acellular capillaries in diabetic retinas and to create a standard for retinopathy assessment. Conclusions: We have designed an automated computer-based system to enumerate the acellular capillaries in diabetic retina. This computer-based automated system will enhance consistency in retinopathy assessment and reduce time for analysis.

Intern: Melanie Scheive  
Major: Neuroscience  
Mentor: Jinhui Chen  
Department: Stark Neuroscience Research Institute  

Determining the Behavioral and Pathological Consequences of Mild Traumatic Brain Injury

Mild traumatic brain injury (mTBI) occurs when a forceful motion of the head region results in a brief alteration of mental status for under 30 minutes. This invisible injury has become a serious public health problem, affecting 75 percent of the more than 1.9 million individuals in the U.S. who experience traumatic brain injury each year. Many victims of mTBI include soldiers and veterans exposed to improvised explosive devices in the battlefield. However, the exact changes in brain function, behaviorally and pathologically, as a result of mTBI in military populations remain elusive. Consequently, this project seeks to determine the behavioral and pathological effects of mTBI at different levels of blast wave exposure using a novel blast wave animal model. The initial baseline injury findings will then be utilized to test potential treatment options before clinical testing can be performed. Through this project, the question of how the brain is affected by mild blast injuries to the head is attempting to be answered. In order to figure out the answer to this question, behavioral testing, including elevated plus maze, open field test, three chamber social memory test, should enable any changes in anxiety and social interaction from the injury to be seen. Additionally, any pathological consequences of mild blast injuries on the brain can be elucidated through immunofluorescence that measures necrotic and apoptotic cell death; microglial, astrocytic, and oligodendrocytic damage; and axonal and dendritic spine degeneration.
Relationship between Latent Viruses in HIV Positive Patients and Chronic Pulmonary Inflammation leading to Further Pulmonary Complications

Background: Highly Active Antiretroviral Therapy (HAART) has dramatically improved the outlook of HIV patients. However, they remain susceptible to lung complications, likely due to persistent chronic lung inflammation. Persistent or latent viruses are able to create an inflammatory response. Therefore we hypothesized that persistent antigenic stimulation by viruses leads to an immunosenescent lung phenotype and chronic lung inflammation, which contributes to the late complications associated with HIV infections. Method: BAL and blood was collected from 17 HIV positive subjects, who underwent Pulmonary Function Testing and CT scanning to determine if they have subclinical pulmonary complication, and 5 normal volunteers. A measurement of secretory cytokine, chemokines and a virome analysis was done on the BAL and blood. Results: 1. The BAL CD4:CD8 ratio was in the normal range and greater than blood. 2. BAL cytokines and chemokines levels remained high in many HIV positive subjects. 3. In HIV positive subjects, CD8+ CD 57+ cells were present suggesting chronic immune activation. 4. Preliminary analysis demonstrates that HIV BAL in which viruses are detected contains higher inflammatory cytokines and chemokines. 5. HIV positive subjects have evidence of airflow obstruction on PFTs. 6. CT scan results are pending. Conclusion: Even after 3 years of effective HAART treatment, evidence of chronic lung inflammation persist and are associated with some pulmonary complications found in HIV positive subjects. Preliminary data suggest that this is due to persistent viruses in the lung causing chronic lung inflammatory responses.

Adolescent Reluctance to Discuss Sexual Topics with Mothers and Perceived Parental Support

Several studies have shown that adolescents’ primary sexual educators are their mothers. Past research has focused on analyzing the amount of sexual topics discussed, the frequency of the discussions, and even the quality of the discussions. However, barriers to communication are also important factors to study. This research intends to discover how adolescent reported reluctance to discuss sexual topics with their mother is related to adolescent-perceived parental support. Data was collected from 100 middle school and high school students at local public schools, as well as from their mother, by administering a survey covering a range of topics including reluctance to discuss sexual topics with mothers, perceived parental support, and family communication about sexual topics. The survey was conducted at 3 time points approximately 90 days apart, although only baseline data was used in this analysis because of the ongoing nature of the study. Correlational analysis suggests that adolescent reluctance to discuss sexual topics with their mothers and perceived parental support have a strong negative correlation ($r=-0.711$, $p<0.001$). Since there is also a strong negative correlation between adolescent reluctance to discuss sexual topics with their mothers and the amount of family communication about sex ($r=-0.269$, $p<0.01$), it is possible that adolescents who perceive little parental support are not receiving as much sexual education from their mothers as those who perceive high parental support.
Investigating the Effects of Hydrocortisone Treatment of ECFCs upon PLAC8 DNA Methylation

Prenatal exposure to gestational diabetes mellitus (GDM) increases the risk of children developing hypertension, obesity, and type 2 diabetes. These chronic conditions may be a result of the altered functioning of endothelial colony forming cells (ECFCs). In GDM ECFCs, the placenta-specific 8 (PLAC8) gene has been found to be overexpressed, and its overexpression contributes to GDM ECFCs’ altered function. Methylation of cytosines (CpGs) has been linked to decreased transcription factor binding and reduced gene expression. Preliminary data indicate the PLAC8 gene has differential methylation at 11 CpG sites in PLAC8 intron 1. Methylation at these sites negatively correlates with PLAC8 RNA levels. Our lab has determined that an important stress hormone, hydrocortisone, increases PLAC8 mRNA. The objective of this study is to determine if treatment with hydrocortisone alters PLAC8 DNA methylation. We predicted that hydrocortisone treated ECFCs will have lower methylation percentages than non-hydrocortisone treated ECFCs in the PLAC8 CpG sites. Bisulfite PCR followed by restriction enzyme analysis was used to measure the percent methylation at one of the 11 previously studied CpG sites. Hydrocortisone-treated ECFCs from a control cell line sample had a 40% methylation in contrast to non-hydrocortisone treated ECFCs with a 50% methylation, leading us to conclude that hydrocortisone treatment may lead to decreased DNA methylation. Further studies are being conducted with additional control and GDM ECFC cell lines to increase the power of our study determining the effect of hydrocortisone on percent methylation. Other studies will examine methylation of other CpG sites in response to hydrocortisone treatment.

Participation in Community-Based Adapted Yoga Improves Balance Scores in Adults With Chronic Stroke: Preliminary Data.

Background: Stroke is a devastating medical event which leads to long-term physical deficits, including impaired balance. Balance impairments can lead to increased fall risk as well as loss of function. Therefore it is important that people with stroke engage in post-rehabilitation activities that can minimize balance impairment. Unfortunately, post-rehabilitation programs to improve balance are not readily available in the community for people with stroke. Purpose: The purpose of this study was to assess the efficacy of a post-rehabilitation community-based adapted-yoga program on balance in people with stroke. Methods: This pilot efficacy study recruited participants through local rehabilitation programs and the YMCA. Participants attended an adapted-yoga class (2X/week for 8 weeks) at the local YMCA. Assessments of balance (Berg Balance Scale (BBS), Dynamic Gait Index (DGI)) were completed at baseline and post-yoga and were analyzed with paired t-tests (p=0.05). Demographic and stroke characteristic data were collected at baseline and were analyzed with descriptive statistics. Results: Nine participants were recruited and 7 (78%) completed the program. Only 6 of the participants were able to complete the standing balance assessments. Those 6 are included in these analyses. The average age of participants was 55 years, and the average time post-stroke was 3 years. Four (66%) participants were male, and 4(66%) had left hemiparesis. Balance measures improved significantly between baseline and post testing (BBS, 35 to 47, p= 0.009; DGI, 13 to 16, p= 0.007). Conclusion: Adapted-yoga as a post-rehabilitation community-based program may be able to improve balance scores in people with chronic stroke.
Intern: Eugene Tandukar  
Major: Biology

Mentor: Komal Kochhar  
Department: Bowen Research Center

Factors influencing the family medicine residents’ decision to practice in Indiana

Background: Having a better understanding of the factors that influence how residents choose a practice location will help improve the efforts to recruit and retain family medicine physicians in areas of need within Indiana.

Methods: In 2014, a cross-sectional survey of all final-year Indiana family medicine residents was conducted. The survey used a group-administered questionnaire to obtain respondents’ demographic characteristics and their plans after graduation, including where they intend to practice and why they chose that specific location. Of the 82 residents graduating from these eleven programs, all were invited to participate on the survey, thereby yielding a 100 percent response rate.

Results: Of all respondents: 63% were between 30 and 34 years old; 49% were female; 83% were white, non-Hispanic; 14% were from another country. Of the respondents from U.S., 51% considered Indiana to be their hometown. After completing their program, 76% expect to be involved in patient care; 94% will work full-time; 62% will stay within Indiana and 33% will relocate to another state; 13% will enter group practice and 62% will enter a hospital setting. Top three reasons for practicing in Indiana: proximity to my family (59%), cost of practicing is reasonable (54%), salary (46%), and cost of malpractice (46%); while the top 3 reasons for choosing not to practice in Indiana were: proximity to my family (41%), proximity to my spouse's family (23%), and climate (23%).

Conclusions: A majority of the respondents intend to practice in Indiana to meet the healthcare needs of their communities.

Intern: Ashley Troutman  
Major: Exercise Science

Mentor: Mary Beth Brown  
Department: Physical Therapy

The Effect of Exercise Training on Skeletal Muscle Fiber Size in a Rat Model of Hypoxic Pulmonary Hypertension

Pulmonary hypertension (PH) secondary to chronic hypoxia increase the work of the right heart and can eventually lead to right heart failure and death. Recent reports indicate that, in addition to cardiopulmonary pathology, skeletal muscle dysfunction may contribute to the exercise intolerance characteristic of patients with PH. The purpose of this research is to determine how aerobic exercise training affects skeletal muscle fiber size and how this relates to measures of aerobic fitness (VO2max) in a hypoxia PH rat model. A 6 wk treadmill (TM) running program (5 sessions/wk @ 75% of VO2max reserve) in normoxia was initiated for male Sprague-Dawley (180-200g) rats (ExT, n=9), progressed up to 60 min/session. Sedentary counterparts (SED, n=7) were placed on a stationary TM on a matched schedule. After 3 wks, housing for a subgroup of ExT (HPH-ExT, n=6) and SED (HPH-SED, n=4) rats was relocated to hypobaric hypoxia (Patm=362 mmHg; 10% FiO2) for the remaining 3 wks of the training program. VO2max was assessed at 3 timepoints via analysis of expired gases: pre-ExT, pre-hypoxia, and post-ExT. At the conclusion of the 6wk ExT program harvested soleus tissues were cryofixed, sectioned, and stained with nuclear and cell membrane specific fluorescent dyes for image capture with epifluorescence microscopy. Mean myocyte area is currently being determined for three stained soleus sections per animal using Image J software. Values will be compared between exercised and sedentary HPH and healthy groups, and additionally analyzed in relation to individual measures of post-training VO2max and total soleus muscle wet weights.
Mechanical effects of fine-wire climbing on the hindlimb skeleton of mice

High-impact exercise can stimulate multiple anabolic responses (increased trabecular bone volume, BV/TV) in the skeleton; it is linked to an increased incidence of skeletal fracture. However, multi-directional off-axis loading events have elicited anabolic responses even when magnitudes are low. This represents a potential alternative to high-impact exercise for improving skeletal mechanical properties. To test this hypothesis, we raised 19 weanling female C57BL/6 mice to skeletal maturity (4 months) in enclosures that prevent (control) or require (experimental) manual and pedal grasping while balancing and climbing above fine wire substrates. At sacrifice, we measured whole mouse bone density (DEXA) and performed architectural (μCT) and mechanical (4-pt bending) analyses of the femur. Body mass was similar between groups, although exercised mice were leaner (-34% fat mass). Bone mineral density and mineral content were similar between the groups. Femoral midshaft polar moment of inertia and cortical area and cortical thickness were also similar between groups, but exercised mice had lower BV/TV (-24%) of the distal femur as a result of fewer trabeculae (-27%). Exercised femora fractured in bending at higher ultimate forces (+17%), although yield forces were not different. Post yield displacement (+70%) and post yield work (+82%) were greater in exercised mice relative to controls. Stiffness and toughness were elevated, but not significantly higher in the exercised mice. These data are consistent with some high-impact exercise regimens, but not others, and suggests that this exercise model may improve bone mechanical properties by redistributing mineral within the bone not by increasing net bone formation.

Paratransit Services: The Experience of Older Adults and Persons with Developmental Disabilities

Background: Community mobility is a concern for people who desire to live independently. Because of their disabling conditions, older adults and persons with developmental disabilities are neither able to drive nor use fixed-route public transportation. Paratransit service is a viable alternative for these two populations. Little research exists that addresses the experience of older adults and those with developmental disabilities using paratransit, and this study aims to rectify the literature gap. Method: Older adults over the age of 65 and people with developmental disabilities were interviewed using a semi-structured interview format. Since context is important for ascertaining the true experience of these people, the researchers chose to utilize a qualitative research approach. Results: After analyzing the interviews, important themes emerged for both populations: loss of time, crowded buses, lifestyle changes, and social participation. However, a distinction arose in the way they viewed their experiences using paratransit: those with developmental disabilities had a concrete outlook and viewed their experiences in a simplistic way, while older adults were more nuanced in their answers. Discussion: Without this transportation, the two populations would not feel as independent or be able to participate in social activities. Although participants reported frustrations while using paratransit systems, they understood the limitations and were simply happy to move around their community. Conclusion: This study concludes that while challenges exist for utilizing paratransit services, the myriad of benefits reported by participants definitely made paratransit a positive experience.
An Integrase-Deficient Lentiviral Vector for Reprogramming Bone Marrow-Derived Cells

BACKGROUND: Systemically injected murine bone marrow-derived cells (BMDCs) reprogrammed to retinal pigment epithelium (RPE) cells via lentiviral (LV) vector-mediated expression of RPE65 repopulate the RPE in a mouse model of retinal degeneration. As LV vectors integrate into coding regions, insertional mutagenesis is a significant safety concern for clinical use. We investigated an integrase-deficient LV vector expressing RPE65 as an alternative, improving vector safety by limiting integration.

METHODS: Vector plasmid pCDH-RPE65 was packaged in 293T cells with VSV-G and pMDL or pMDL-D116N (integrase-deficient) packaging plasmids. Vectors were characterized in murine lin-/-Sca1+ BMDCs isolated from total bone marrow using EasySep magnetic beads (negative selection for lin- followed by positive selection for Sca1+). Cells were transduced at an MOI of 50 on RetroNectin for 2h at 150g, 16h before analysis. Expression of human and murine RPE65 and the RPE cell-specific marker CRALBP were determined by qRT-PCR. Untransduced lin-/-Sca1+ cells were used as a negative control.

RESULTS: pCDH-RPE65 can be packaged as an integrase-deficient vector. Compared with integrating pCDH-RPE65, pCDH-RPE65Δint transduction efficiency is 10-fold lower. However, expression of the endogenous murine RPE65 gene is increased 4-fold over the negative control in cells transduced with either pCDH-RPE65Δint or pCDH-RPE65. CRALBP expression is 5-fold higher than the negative control in cells transduced with either pCDH-RPE65Δint or pCDH-RPE65.

CONCLUSIONS: BMDCs transduced with the integrase-deficient RPE65 vector display similar characteristics to BMDCs transduced with integrating RPE65 vectors, indicating that this vector may be sufficient to

Intern: TaNesha Williams
Major: Psychology
Mentor: Derek Jahnke
Department: Neuroscience

Reducing the Incidence of Skin Breakdown in Neurotelemetry Patients

Introduction: Contact dermatitis and EEG electrode pressure induced wounds are a growing concern for Neurotelemetry patients as the utility of Neurotelemetry increases nationwide. These injuries can lead to infections and increased length of hospital stays. Our objective is to identify key risk factors in Neurotelemetry patients that could help reduce and prevent the incidence of contact dermatitis, skin breakdown, and EEG electrode pressure induced wounds. The Braden Scale scores are being evaluated to determine if it is a significant factor in predicting risk and if any of the subcategories are of prognostic value.

Methods: A study of Neurotelemetry patients is being conducted to understand contributing factors. Currently, retrospective data collection of Braden Scale scores is taking place along with factors such as length of recording, patient description and demographics, nutrition information, medical history, and electrode site description are being collected. A sample of 32 patients with skin breakdown and a control population of 32 patients with no breakdown were analyzed along with comparisons between the subcategories of mobility, activity, sensory perception, moisture, nutrition, and friction and shear.

Results: The averaged total Braden Scale scores and subcategories for those with skin breakdown and those without as well as the difference between the patient groups is listed in the table below.

Conclusion: The average difference between the patient groups show that patients with no skin breakdown have a higher score and that the subcategories of moisture, mobility and sensory perception may be indicators of increased risk. Further analysis is needed to determine the prognostic value.
Investigating Phosphate and Fgf23 in the Development of Left Ventricular Hypertrophy in Chronic Kidney Disease

Chronic kidney disease (CKD) is a common condition affecting many Americans. Fgf23 is a hormone elevated in those with CKD to enhance the excretion of phosphate from the body. However, the kidneys do not perform optimally in CKD, inhibiting the ability of Fgf23 to execute this function. Previous research indicates that high levels of Fgf23 may play a role in the development of left ventricular hypertrophy (LVH) in CKD. Still, additional factors, such as hyperphosphatemia, may also contribute to LVH in CKD. This study aimed to remove phosphate as a factor in LVH such that any change in heart size could be attributed to Fgf23. As an animal model of CKD, we used Juvenile cystic kidney disease (Jck) mice, which have progressively reduced kidney function like someone with CKD. Jck mice were mated to Galnt3 knockout mice, which have reduced Fgf23, to generate four groups: Galnt3 mutant, Jck mutant, double mutant, and phenotypically normal mice. From these four groups, the mice were split into two groups: one with a normal (0.60%) phosphate diet and the other with a low (0.10%) phosphate diet. The blood and hearts were collected from 12-14 week old mice. The Jck mutant and double mutant mice exhibited elevated expression in common LVH gene markers. Serum analysis indicated the restoration of inorganic phosphate to normal levels after reducing dietary phosphate in Galnt3 and double mutant mice. Also, Fgf23 levels declined in all mice on the low phosphate diet. Despite these changes in serum phosphate and Fgf23, the LVH markers in mutant mice remained higher than normal mice. These data suggest that factors other than Fgf23 and hyperphosphatemia may contribute to development of LVH in CKD.

Preventing late-life disability through 3-Step Workout for Life

The purpose of this study is to prevent late life disability. The literature has shown that as we age, our muscles start to atrophy. Muscle weakness is strongly linked to falls and disability in older adults. Based on exercise science and rehabilitation science, 3-Strep Workout for Life focuses on the dual goals of improving muscle strength and the ability to perform activities of daily living. The intervention is a ten week process of therapeutic home exercise. The “three step” consist of muscle strength training, function training, daily activity training. Muscle strength training works on strengthening major muscle groups of the upper and lower extremities. Functional training works on practicing common movement patterns used to perform activities of daily living. Daily activity training works on “exercising” daily tasks that older adults need to do in order to live independently. A trainer delivers the intervention in the participant’s home. The purpose of this study is to test whether 3-Step Workout for Life helps older adults prevent late-life disabilities so they can age-in-place and enjoy their life. Evaluations are conducted before and after the intervention to measure the training effect on functional outcome.
LHSI Alumni Posters

LHSI is proud to have 8 posters from alumni of the program. These are former interns who completed their internships in the 2013-2014 cohort or before. Many of these students continue to work for their LHSI mentors as research assistants or hourly employees, or in other capacities on campus.

Intern: Ira Altaras
Major: Biology
Internship Year: 2013-14

Mentor: Lyne Racette
Department: Ophthalmology

A pilot study of the effectiveness of motivational interviewing to improve adherence to glaucoma treatment in patients of African descent

The first line of treatment for open-angle glaucoma is the use of daily hypotensive eye drops to control intra-ocular pressure. Adherence to this treatment is known to be challenging for patients, and has been reported to be worse in patients of African descent (AD), a segment of the population that is disproportionately affected by the disease. Motivational interviewing (MI) can improve adherence and has been shown to be more effective in minority populations. The purpose of this prospective, longitudinal and interventional pilot study was to determine whether MI might improve adherence in glaucoma patients of AD. Thirteen patients of African descent (AD) who received a clinical diagnosis of open-angle glaucoma within the past five years were included in this study. All patients used once-daily prostaglandin analog eye drops and administered their medication. Adherence was measured using Medical Event Monitoring System (MEMS) bottles. The cap of these bottles electronically records the date and time at which the bottle is opened. At visit 1, patients were instructed to place their eye drop bottle in the MEMS bottle and to otherwise use their eye drops as usual. At the 4-weeks visit, baseline adherence was assessed. Patients with adherence levels below 75% (n=9) received an approximately 20-minutes MI intervention and those with adherence levels over 75% served as controls (n=4). At the 12-weeks visit, patients returned and the final adherence was assessed. Baseline and final adherence were compared in each group and the difference between baseline and final adherence was compared between the groups using one-tailed paired t-tests.
Intern: Hardeep Dhillon  
Major: Biology, Neuroscience  
Internship Year: 2012-13

Mentor: Randall Roper and Charles Goodlett  
Department: Orthopedics

Effects of Increased Dosage EGCG Treatment on Cognitive Deficits in the Ts65Dn Down Syndrome Mouse Model

Down syndrome (DS), a trisomy of human chromosome 21 (Hsa21), is the leading genetic cause of cognitive impairment and results in a constellation of phenotypes. Although symptomatic treatments exist for DS phenotypes, treatments generally do not address the genetic etiology. The Ts65Dn mouse model, with a triplication of approximately half the gene orthologs of Hsa21, exhibits hippocampal learning and memory deficits as well as cerebellar motor and spatial deficits similar to individuals with DS. DYRK1A, one of the genes overexpressed in DS, has been identified as a potential cause of cognitive impairment; therefore normalization of DYRK1A activity may be a valid form of treatment. We have shown that Epigallocatechin-3-gallate (EGCG), a major polyphenol of green tea, can rescue skeletal deficits in Ts65Dn mice at a low dosage. When this same low dosage was used to rescue behavioral deficits, however, it was ineffective. We hypothesize that high dose EGCG treatment lasting throughout behavioral testing will rescue the cognitive deficits observed in Ts65Dn mice. Trisomic mice and euploid littermates were given EGCG or water for 7 weeks while being tested sequentially on novel object recognition (NOR) and Morris water maze (MWM). Our current data shows that Ts65Dn mice exhibit deficits in learning and memory; further data will be collected to identify the effect of EGCG. Data showing pure EGCG as being ineffective will suggest the importance adding a supplemental compound, while data showing pure EGCG as an effective form of treatment will support use of EGCG in translational studies in humans.

Intern: Jeffery Joll  
Major: Biomedical Engineering  
Internship Year: 2013-14

Mentor: Jason Organ  
Department: Anatomy and Cell Biology

Mechanical effects of fine-wire climbing on the hindlimb skeleton of mice

High-impact exercise (running/jumping) stimulates anabolic responses (increased trabecular bone volume, BV/TV) in the skeleton, but is also associated with higher incidence of skeletal fracture. Thus, it is not an appropriate treatment for patients with an elevated risk of fracture. Mechanical loads originating from multiple, off-axis directions, however, have elicited anabolic responses even when magnitudes are relatively low. This represents a potential alternative to high-impact exercise for improving skeletal mechanical properties. To test this hypothesis, we raised twelve weanling female C57BL/6 mice to 4 months of age in custom enclosures that prevent (control) or require (experimental) manual and pedal grasping while balancing above narrow wire substrates. At sacrifice, we measured whole mouse bone density (DEXA) and performed architectural (μCT) and mechanical (4-pt bending) analyses of the femur and tibia. Body mass was similar between groups, although exercised mice were leaner (-35% fat mass). Bone mineral density was also similar, while bone mineral content was increased (+7%) in the exercised mice. Midshaft femoral polar moment of inertia was similar between groups, but exercised mice had lower BV/TV (-46%) of the distal femur with greater trabecular spacing (+21%). Bone mineral density was also similar, while bone mineral content was increased (+7%) in the exercised mice. Midshaft femoral polar moment of inertia was similar between groups, but exercised mice had lower BV/TV (-46%) of the distal femur with greater trabecular spacing (+21%). Exercised femora showed more total displacement (+58%) and post yield displacement (+115%) in bending than controls, and increased material toughness (+40%). Patterns were similar for the tibia. Mechanical data are consistent with high-impact exercise studies, but architectural data are not. Together they suggest that our exercise model may improve bone mechanical properties by redistributing mineral within the bone, and not by increasing net bone formation.
Intern: Janine Kabir  
Major: Biology  
Internship Year: 2013-14  

Mentor: Angela Bruzzaniti  
Department: Oral Biology

The Effect of Presenilin on Osteoblasts.

A characteristic of osteoporosis is lower bone mass. A decrease in bone mass can result from dysfunctional osteoblasts (OB), cells that form bone, or osteoclasts, cells that degrade bone. Alzheimer’s Disorder is a neurodegeneration disease known to cause amyloid plaques in the brain, which is thought to be regulated by Presenilin (PS1). Presenilin is also known to be linked to the development of the central nervous system. In AD patients, Presenilin is abnormal due to a point mutation PS1-L166P, which is the protein of focus in this research. A recent clinical study has found that patients with Alzheimer’s Disorder have a lower bone mass. We found that mice harboring the PS1-L166P genetic mutation found in humans also have low bone mass. We hypothesize that the activities of Presenilin may control the activities of OB, leading to the low bone mass PS1-L166P knock-in mice. This study focuses on understanding the role of PS1 on OB function. Polymerase chain reaction analyses confirmed the expression of PS1 in OBs grown in osteogenic media from day 0 to day 14. In addition, ALP and mineralization assays were performed to examine the function of OB. Preliminary data demonstrates that OBs from PS1 mice have a decrease in mineralization and ALP activity. This data suggests that the low bone mass of PS1-L166P mice may be in part due to decreased OB activity. Understanding the function of PS1 may one day lead to therapeutic treatments to restore bone mass in patients with AD and osteoporosis.

Intern: Zia Nuss  
Major: Chemistry  
Internship Year: 2012-13  

Mentor: Emily Blue and Laura Haneline  
Department: Pediatrics

Epigenetic PLAC8 Gene Regulation of Intrauterine Diabetes Exposed ECFCs via DNA Methylation

Gestational diabetes mellitus (GDM) is defined as impaired glucose tolerance diagnosed during the third trimester of pregnancy. GDM occurs in about 10% of pregnancies. Children of diabetic mothers have an increased risk of high blood pressure, diabetes, and obesity later in life. Endothelial colony forming cells (ECFCs) play an important role in blood vessel growth and repair. If dysfunctional, ECFCs are likely to contribute to maladies. ECFCs previously exposed to intrauterine diabetes are abnormal displaying increased proliferation and decreased angiogenesis. Placenta-specific gene 8 (PLAC8) mRNA and protein levels are upregulated in many GDM exposed ECFCs. Relevant to our findings, PLAC8 is known to increase proliferation, but how PLAC8 expression is regulated is unknown. Increased methylation of CpG residues in promoter regions and in CpG islands often resulted in reduced gene expression. We hypothesized that intrauterine exposure to diabetes led to decreased CpG methylation of the PLAC8 promoter, causing decreased PLAC8 mRNA expression. To test this, RNA and DNA were collected from control and GDM ECFCs isolated from human cord blood. The levels of PLAC8 mRNA were analyzed by quantitative RT-PCR. Methylation of genomic DNA was assessed using bisulfite sequencing. CpG sites in the putative PLAC8 promoter region show hypomethylation in GDM-exposed ECFCs. There was a significant, negative correlation between relative PLAC8 mRNA levels and DNA CpG methylation at 17 CpG sites (n=18). In conclusion, PLAC8 gene expression is likely regulated epigenetically. Future studies include transcription factor binding assays for the PLAC8 promoter region.
A longitudinal evaluation of the spatial concordance in location of visual field defects in glaucoma

Purpose: Glaucoma presents bilaterally in many patient, with a lag between presentation in the right and left eyes. In this analysis performed on the prospective data collected in an observational study, we assessed whether the overlap in the location of abnormal visual field (VF) between the right and left eyes increases over time. Methods: The dataset included 97 patients diagnosed with primary open-angle glaucoma were selected from the Diagnostic Innovations in Glaucoma Study (DIGS) and from the African Descent and Glaucoma Evaluation Study (ADAGES). The eye with the more advanced visual defect was selected as the reference eye (RE). The RE had a repeatable defect defined as a cluster of at least three points and no more than 26 abnormal points on the pattern deviation plot (PDP). The fellow eye (FE) had at least ten follow up visits separately by at least 5 months. The VF of the RE was compared to each consecutive VF in the FE. The inter-eye concordance (IEC) ratio was calculated using this formula: \(2C/(A+B+2C)\), where A represents locations abnormal in the right eye only, B represents locations abnormal in the left eye only, and C represents locations abnormal in both eyes (Boden et al, Ophthalmology, 2006; 113:918-23). Results: Overall, a slightly positive mean slope was obtained (0.00003). Although the mean slope was small, it was positive as expected if the IEC increases over time. Conclusions: Inter-eye concordance increased slightly over time and more patients positive than negative slopes. The small slopes we obtained are in part due to the strict criteria we used for concordance given the known variability present in visual fields: the exact same location had be abnormal.

A Double-Blind Trial of Adjunctive Valacyclovir to Improve Cognition in Early Phase Schizophrenia

Schizophrenia is a chronic and debilitating neuropsychiatric disease that occurs in approximately one percent of the population and is characterized by difficulties with discerning reality from fiction, abstract thinking, and effective communication. Cognitive impairments are a prominent feature of the illness and contribute to significant occupational and social disabilities. Additionally, cognitive symptoms often do not subside with the disappearance of psychotic symptoms, and there have been no clearly effective treatments discovered to treat them. Although the etiology of cognitive impairment in schizophrenia is unknown, recent studies have shown an association between Herpes Simplex Virus 1 (HSV-1) exposure and the severity of cognitive impairments in the schizophrenic population. Valacyclovir is an oral antiviral medication approved by the United States Food and Drug Administration for treatment of herpes virus infections, including HSV-1. A recent pilot study at the University of Pittsburgh found that treatment of schizophrenic patients with adjunctive valacyclovir improved working and visual memory in comparison to placebo. However, this study did not include a HSV-1 seronegative group, and it could not be determined if the seropositivity of subjects contributed to positive cognitive results. The primary goal of our study is to determine the efficacy of adjunctive valacyclovir to improve visual and working memory in HSV-1 positive individuals with early phase schizophrenia. This poster presents a comprehensive review of recent findings regarding the importance of HSV-1 infection and inflammatory markers in schizophrenia, and discusses the methods and expected outcomes of our ongoing study.
Vision

To be the destination for IUPUI life and health sciences undergraduates to participate in enriching experiences in laboratories, research projects, and other professional experiences on the IUPUI campus and in campus-affiliated locations.

Mission

To educate, engage, and enlighten IUPUI life and health sciences undergraduates through on-campus internship experiences. We seek to achieve this through the following means:

1. Arranging high quality internship opportunities in relevant fields.
2. Nurturing mentor and intern relationships through structured meetings, gatherings, and professional development opportunities.
3. Providing opportunities and support to present work.

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