IUPUI Life-Health Sciences Internship Program

Spring 2014 Poster Session

Friday, April 25, 2014
3:00 PM—5:00 PM
VanNuys Medical Science Building Atrium
Welcome to the IUPUI Life-Health Sciences Internship Program Spring 2014 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 the IUPUI Commitment to Excellence grant.

Life-Health Sciences Internship students represent 12 different majors across eleven 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 other research and internship opportunities as well as graduate and professional programs.

Mentors are faculty and staff within Indiana University School of Medicine, Indiana University School of Dentistry, Indiana University School of Health and Rehabilitation Sciences, Indiana University School of Nursing, and Indiana University Health. These professionals are providing invaluable experiences for undergraduate students and mentoring the next generation of scientists, researchers, and health professionals.

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 2013-2014 participants:

**Interns**

- Paige Allen
- Ira Altaras
- Susanna Angermeier
- Gracelyn Bose
- Hailey Campbell
- Kelsey Downham
- Taylor Duncan-Presson
- Melissa Gronceski
- Maria Harlan
- Brandi Herron
- Garret Hillsdon-Smith
- Abigail Huffer
- Sarah Islam
- Jeffery Joll
- Janine Kabir
- Mai Khuu
- Sharifah Kyazike
- Alexa Lahren
- Katharina Lane
- Elizabeth McIntyre
- Jeremy Mihajlovich
- Mohamed Mohamed
- Hunter Muhney
- Haley Neal
- Rachel Novack
- Jason Olson
- Jaymin Patel
- Anjali Prakash
- Heather Reeves
- Emalee Reichenbach
- Gregory Rothchild
- Mehdi Shadmand
- Ankita Sutaria
- Sarah Torline
- Roziya Tursunova
- Leah Van Antwerp
- Piiamaria Virtanen
- Whitney Walker
- Angela Wallen
- Kamilah Walters
- Ellie Weber
- Megan Welch
- John Wells
- Weston Wright
- Dana Yenko
- Lauren Yoder

**Vision**

The Life-Health Sciences Internship Program connects talented IUPUI undergraduate students in the life and health sciences with 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. Seeking out and arranging high quality internship opportunities in relevant fields.
2. Nurturing mentor and intern relationships through structured meetings and gatherings.
3. Providing opportunities and support to present work.

*The IUPUI Life-Health Sciences Internship Program is funded by the Indiana University Commitment to Excellence Grant.*
Perceived Relationship Control and Adolescent Sexting Behavior

“Sexting” is the use of technology to create, send, and receive sexually suggestive photos or text messages via cell-phone. Sexting by adolescents often results in bullying, harassment, and potential legal ramifications. To combat this problem, it is crucial to examine the motives of adolescents participating in sexting. There has been limited research on the relational contexts in which sexting occurs among adolescents. Even less is known about the role of relationship dynamics (such as perceived relationship control) in the decision to engage in sexting, especially among younger students. Here, middle and high school students (n=493, 38% Caucasian, 45% African American, and 17% other) completed a questionnaire assessing perceived relationship control (scale 1-10, with greater scores indicating a sense of control), attitudes about abstinence, condom use, and specific sexual behaviors. Females tended to score higher on perceived relationship control, (middle school males and females; 7.6, 9.7; high school males and females; 7.9, 8.8). Bivariate correlations indicated that greater perceived relationship control was significantly related to less sexting among older females (r = -0.27, p<0.05). In contrast, for high school males, greater perceived relationship control was correlated with higher rates of sext message receipt (r = 0.17, p<0.01). While these associations were not found among middle school students, the prevalence of sexting among younger students was far less than older students. The association of sexting with relationship control provides potential answers as to what makes a student more or less likely to participate in sexting.
Intern: Dana Yenko  
Major: Forensic Science and Criminal Justice

Mentor: Shoji Ichikawa  
Department: Endocrinology

Effect of parathyroid-specific Klotho deletion in a murine model of CKD

Fibroblast growth factor 23 (FGF23) is a hormone made in osteoblasts and osteocytes and increases phosphate excretion in the kidney. For FGF23 to maximally function, the fibroblast growth factor receptor (FGFR) must be paired with a coreceptor encoded by the Klotho gene. Parathyroid hormone (PTH) secreted by the parathyroid gland also has a phosphaturic effect; however, it is the primary regulator of serum calcium. Together, PTH and FGF23 work to maintain calcium and phosphate homeostasis in the body. It has long been thought that there is a link between the levels and functions of each hormone. PTH stimulates FGF23 production in bone, while FGF23 may inhibit PTH secretion. However, in patients with chronic kidney disease (CKD), both PTH and FGF23 are markedly elevated. To determine the effect of FGF23 on PTH secretion in CKD, we used juvenile cystic kidney disease (Jck) mutant mice as a model of CKD. Jck mutant mice were crossed to PTH-Cre mice to conditionally knock out the Klotho gene in the parathyroid gland. Mice were weighed biweekly, and the changes in the serum levels of alkaline phosphatase, calcium, creatinine, BUN, and phosphorus were measured at 12 weeks of age. Jck mutant mice were significantly smaller than normal mice at 12 weeks. As expected, Jck mice had significantly elevated levels of serum BUN, a marker of kidney function. In addition, serum calcium was slightly elevated in Jck mice with Klotho, while it was normal in Jck without Klotho. The difference in serum calcium levels suggests that FGF23 and Klotho may be important in the regulation of PTH secretion and calcium homeostasis.
Osteoblast-specific Overexpression of Human WNT16 Increases both Cortical and Trabecular Bone Density and Improves Bone Structure in Mice

Osteoporosis is a common bone disease that is characterized by a decrease in bone mineral density (BMD) leading to an increased susceptibility to fracture at multiple skeletal sites. Osteoporosis affects nearly 50% women and about 20% of men. As much as 80% of the variability in peak BMD is attributable to genetic factors. A recent genome-wide association study involving over 40,000 patients identified SNPs in WNT16 that were associated with BMD and risk of fracture, and thus WNT16 was chosen for this study as a likely contender in the formation of bone. To further identify the role of WNT16 in bone mass regulation, we created transgenic (TG) mice over-expressing human WNT16 in osteoblasts on B6 background. Compared to wild-type (WT) mice, WNT16-TG mice exhibited significantly (p<0.0001) higher whole body aBMD and BMC at 6 and 12 weeks of age in both male and females. µCT analysis of trabecular bone at distal femur revealed significantly (p<0.0001) higher BV/TV, Tb.N, Tb.Th but lower Tb.Sp in TG mice compared to WT littermates. The cortical bone at the midshaft femur also showed significantly (p<0.005) higher BA/TA and cortical thickness in the TG mice. Serum biochemistry analysis at 12 weeks of age showed that both Ca and P levels were similar between WT and TG mice. Male TG mice also had 20% higher serum ALP and 23% higher OC compared to WT mice. In addition, 14% (male) and 22% (female) lower CTX/TRAPc5b ratio was observed in TG mice compared to WT animals, suggesting that WNT16 affects both bone formation and resorption parameters. Our data indicates that WNT16 is critical for positive regulation of both cortical and trabecular bone mass and structure, and that this molecule can be targeted for therapeutic interventions to treat osteoporosis or other low bone mass and high bone-fragility conditions.
Do visual field defects occur in the same location in both eyes in glaucoma?

Glaucoma is an eye disease in which the retinal ganglion cells and their axons slowly degenerate leading to irreversible vision loss. While one eye is typically affected first, the fellow eye will be also be affected eventually. The purpose of this cross-sectional study was to determine whether the defect location in the eye affected first could predict the location of the defect in the fellow eye. A secondary goal was to determine the mechanism underlying the spatial correspondence of visual defect between the eyes. This study included 747 patients from the Diagnostic Innovations in Glaucoma Study and African Descent and Glaucoma Evaluation Study. The visual fields (VF) in each eye were matched in two different ways to determine whether inter-eye concordance (IEC) was driven by the optic nerve anatomy (ONA) (as described in Boden et al, 2006) or by a top-down process (TDP) from the central nervous system, as recently proposed by Sponsel et al (2014). For both methods, IEC ratio was calculated by dividing the number of locations that were defective in both the left and right eye by the total number of defect locations. The mean IEC ratios were 0.20 and 0.17 for the ONA and TDP methods, respectively. Overall, IEC ratios were smaller using the TDP approach compared to the anatomical approach. Overall, the concordance of visual field defects between the two eyes was relatively low for both approaches. Our results suggest that damage may not always occur at the same location in the visual field.
Intern: Megan Welch  
Major: Forensic and Investigative Sciences  
Mentor: Alexander Obukhov  
Department: Cellular and Integrative Physiology

Diabetic environment down-regulates TRPV1 activity in DRG neurons

The transient receptor potential vanilloid type 1 (TRPV1) is a Ca2+ permeable cation channel that can be activated by heat, acid, and capsaicin. TRPV1 channels reside on the nerve endings and somas of sensory Dorsal Root Ganglion (DRG) neurons and are implicated in pain sensation. Individuals with end-stage diabetic peripheral neuropathy present with decreased pain sensation in the lower extremities innervated by DRG neurons. However, the mechanisms underlying such dysfunction are poorly understood. Here we tested the hypothesis that a diabetic environment alters the function and expression of TRPV1 in DRG neurons, which may ultimately affect pain sensation. A diabetic environment was simulated by culturing DRG neurons in a high glucose medium (25 mM of glucose, HG-DRG neurons) for 5-7 days. TRPV1-mediated intracellular Ca2+ increases normalized to the peak amplitude of voltage-gated Ca2+ channel-induced Ca2+ increases were significantly smaller in HG-DRG neurons as compared to control DRG neurons (P<0.001). However, the immunohistochemistry data indicated that TRPV1 expression levels were not different in high glucose-treated versus control DRG neurons (P<0.122). Since a high glucose environment led to an increase in hydrogen peroxide (H2O2) production in the DRG neurons (P<0.001), we tested whether H2O2 affects the function of TRPV1. Electrophysiological data indicated that H2O2 stimulated TRPV1 activity in HEK cells transiently expressing the channel. We propose that increased H2O2 production in HG-DRG neurons results in TRPV1 activation and the channel facilitated Ca2+-dependent desensitization. This may account for the inhibitory effect of high glucose on the function of TRPV1 channels in DRG neurons.

Intern: Susanna Angermeier  
Major: Mechanical Engineering  
Mentor: Yuichiro Takagi  
Department: Biochemistry

Nanobody-aided X-ray Crystallography of Mediator-RNA Polymerase II Complex

Eukaryotic gene transcription by RNA polymerase II (Pol II) accounts for almost all biological activities. Mediator is the key regulator of Pol II. As revealed by the Takagi laboratory using X-ray crystallography and cryo-EM, the essential sub-complex of Mediator termed Head module interacts directly with Rpb4-Rpb7 subunits of Pol II. Mediator-Pol II interaction constitutes fundamental mechanism of gene transcription. Therefore, structure determination of the Mediator Head-Rpb4-Rpb7 complex proves essential. Since Head-Rpb4-Rpb7 complex elicits conformational flexibility, and stabilization of the complex is critical for crystallization, rigidifying the complex is crucial. To this end, the nanobody technology invented by the Steyaert’s laboratory is applied by which the complex can be rigidified by binding of an engineered single viable domain antibody termed nanobody. Binding of nanobodies to the complex will likely generate the uniform sample that is key to obtaining highly diffracting crystals for structure determination by X-ray crystallography. In collaboration with the Steyaert’s laboratory, the DNA library encoding specific nanobodies against the Head-Rpb4-Rpb7 complex has been generated.&nbsp; A total of 52 nanobody-encoding plasmid DNAs were expressed in bacteria followed by Ni affinity purification for all 52 nanobodies.&nbsp; Selected nanobodies have been tested for their abilities to stabilize the Head-Rpb4-Rpb7 complex. Our effort will lead to successful crystallization of the Head-Rpb4-Rpb7-nanobody complex for a structure determination by X-ray crystallography.
Role of Transforming Growth Factor Beta2 in Congenital Heart Disease

Congenital heart disease (CHD) represents the largest class of birth defects in the US and affects about 0.8% of all babies born. About 14 of the CHD patients have structural anomalies of one or more heart valves. As a result of remarkable advances in the medical and surgical management of CHD, more than 75% of children born with CHD now live into adulthood. A recent estimate suggests that approximately 21 million adults are living with CHD and that this population is increasing by 5% per year. As such, discovery of the causes for CHD is not only a fundamental research endeavor, it is vital to the healthcare of this growing community. Inherited genetic mutations in Transforming Growth Factor Beta (TGFβ) gene are found in the patients of Loeys-Dietz syndrome. Several cardiac (endocardial, myocardial) and extra-cardiac (second heart field, neural crest) cell lineages that express Tgfb2 contribute to heart development. To study the role of Tgfb2 in different cell types involved in heart development, we have generated Tgfb2 conditional knockout mice. These mice harbor Tgfb2 LacZ-tagged conditional-ready allele (also called tm1a). By using long range PCR (LR-PCR) we have confirmed the germline transmission of Tgfb2tm1a allele. Histological examination shows that Tgfb2tm1a/tm1a embryos develop several congenital heart defects. This indicates that Tgfb2tm1a allele is a knockout-first allele, which is consistent with the original design of our conditional gene targeting scheme. Next, by crossing to Flp recombinase mice we are able to generate mice with a Tgfb2 conditional-ready allele (also called tm1c). The presence of Tgfb2tm1c allele in the mice is confirmed by genomic PCR that specifically identify tm1c allele.

Plastination of Human Tissues. A Cleaner and Biological Safer Method of Gross Tissue Preservation

Plastination is a technique used to preserve the body or body parts by replacing water and fat with certain plastics that allow the specimens to retain original properties. There is no decay or smell and the specimens can be physically touched and examined after this process is complete. In this study, we examined 200 plastinated specimens and compared them to tissues left in formalin. The formalin fixed specimens have been stored in the solution for about 40-70 years. We found 4 differences between plastinated specimens and long term storage of specimens in formalin while observing in this study. Plastinated tissues maintain shape and organ size significantly better than formalin fixed tissues. The specimens that underwent plastination did not pose an environmental hazard to nose, eyes, or mouth and were also not a cancer threat when exposed. However, formalin fixed tissues are a cancer hazard when exposed and should be handled under a hood with protective eye wear and gloves. Plastinated specimens can be touched, handled, and squeezed without any damage to the tissues while doing such on soft tissues, like those stored in formalin, will breakdown upon handling. In summary, plastination is an excellent modality in preserving organs and tissues in pathology education and teaching. Formalin fixation has been useful in the past 150 years but is not as environmentally safe in contrast to plastination for hands on experience.
Psychotic disorders are characterized by abnormal thoughts and perceptions. Patients with these disorders often experience difficulty in abstract thinking, communicating effectively, expressing emotion, and discerning reality from fiction. Symptoms of psychosis generally present in late adolescence or early adulthood, during which time many executive and emotional neurodevelopmental changes are taking place. Although some psychotic patients experience relatively normal adjustment and functioning prior to symptom onset, many patients and families report noticeable abnormalities earlier in childhood and adolescence. The objective of this study was to identify a correlation between premorbid adjustment and severity of psychosis at disease onset. Data was collected from new patient intake files at the Prevention and Recovery Center for Early Psychosis (PARC) located in Eskenazi Health Hospital. Criteria for acceptance at PARC include being between the ages of 16 and 30, having an onset of psychotic symptoms within the last 2 years, and experiencing impairment in school/social/work function or having suspected prodromal stage of schizophrenia. Each subject was scored using the Premorbid Adjustment Scale (PAS) and the Clinical Global Impressions Severity Scale (CGI-S), and a correlational data analysis was performed. The PAS is used to assess a subject’s social and academic function before the onset of psychotic symptoms, and the CGI-S is used to assess illness severity. Results showed no statistically significant correlation between the two scores, however, further studies regarding premorbid adjustment and the progression of psychotic disorders will be important to refine early intervention approaches and treatments in programs like PARC.
Catsatonia in Two Populations with Psychosis

Schizophrenia is a debilitating mental illness affecting approximately 70 million people worldwide and is characterized by persisting psychosis (cognitive, behavioral, and perceptual dysfunction). Catatonia, a syndrome associated with schizophrenia, is categorized as a disruption of thought and psychomotor processes, but while catatonia can impact diagnosis and treatment, the condition is often overlooked in the context of psychosis. The purpose of this study is to assess the occurrence of catatonic symptoms in two populations of people who have been diagnosed with psychosis. Chronic, intermediate-term inpatients from a state hospital were compared to stable outpatients with sub-optimally controlled symptoms participating in an outpatient research protocol with a catatonia screening tool known as the Bush-Francis Catatonia Screening Instrument (BFCSI). We hypothesized that inpatients would score higher on the BFCSI than the sub-optimally controlled outpatients, and the prevalence of positive screens would be higher in the inpatient group. As hypothesized, inpatient subjects had greater \( p = 0.00001 \) BFCSI scores (mean = 3.1, SD = 1.9) than outpatient subjects (mean = 0.3, SD = 0.6), and inpatients were more likely \( p< 0.00001 \) to have a positive BFCSI. These findings suggest that catatonia screening should be part of the evaluation for those suffering from chronic psychotic conditions as such screening could impact diagnosis and treatment; whereas in stable outpatients, such screening is unlikely to significantly impact diagnosis or treatment.
GATA-1 Deficiency Rescues Trabecular but not Cortical Bone in OPG Deficient Mice

GATA-1low/low mice show an increase in megakaryocytes along with an increase in trabecular bone. This increase in trabecular bone is thought to be due to osteoblastic bone formation being directly stimulated by and osteoclastogenesis being inhibited by megakaryocytes. It is known that osteoclastogenesis is inhibited by Osteoprotegrin (OPG) and, as a result, reduced trabecular and cortical bone is seen in OPG-/- mice due to increased osteoclastogenesis. In addition, it is of note that OPG levels are increased in GATA-1low/low mice. The intention of this study was to ascertain if the osteoporotic bone phenotype in OPG-/- mice could be rescued using a GATA-1 knockdown by breeding GATA-1low/low mice with OPG-/- mice. Similar to OPG-/- mice, GATA-1low/low X OPG-/- mice showed an increase in cortical bone porosity and both types of mice were found to have increased, localized, cortical bone osteoclasts, which may have produced the observed elevated porosity. OPG-/- and GATA-1low/low X OPG-/- femurs were shown to be weaker and less stiff in biomechanical assessment than C57BL/6 or GATA-1low/low femurs. However, the trabecular bone parameters of GATA-1low/low X OPG-/- mice were not different from C57BL/6 values, suggesting that trabecular bone loss observed with OPG deficiency can be partially rescued by GATA-1 deficiency. This indicates that because GATA-1 deficiency partially rescues trabecular but not cortical bone phenotype, MKs may be able to enhance trabecular bone volume locally but the factors secreted by MKs cannot access cortical bone well enough to inhibit osteoclastogenesis or that OPG is required to inhibit cortical bone osteoclastogenesis.

Relationship Between Violence, Childhood Abuse, and Drug abuse Among Early Psychosis Subjects

Schizophrenia is a complex disorder with a wide range of speculated causes. Previous research has linked violent behavior in subjects with a co-occurring diagnosis of substance abuse and early psychosis (Monahan, et al., 2001). Among additional variables other studies have also suggested this correlation. A recent study of 118 participants with a history of abuse (physical, sexual, and emotional) and legal issues, of those participants, 69.6% reported verbal and physical aggression and 61% reported substance abuse tendencies (Spidel, et al., 2010). A correlational analysis was conducted on first- episode psychosis subjects at the Prevention and Recovery Center for Early Psychosis (PARC). Seventy subjects from PARC were selected for further data analysis using demographic and clinical data from clinical charts. A chi-square test of independence was performed to examine the link between each variable of interest (childhood abuse and drug use) and violent behavior. The relationship of these variables to suicidal behaviors was also examined. Childhood abuse and history of drug use were both related to violence and to self-directed violence (suicide attempts and self-mutilation/ injury). Our results are consistent with prior studies evaluating violence in subjects with psychosis. In addition, the link between suicide attempts, self-injury and psychosis is interesting and would be a potential area for more in-depth study.
**Intern:** Melissa Gronceski  
**Major:** Biology and Neuroscience  
**Mentor:** Tamara Hannon  
**Department:** Department of Pediatrics, Division of Pediatric Endocrinology and Diabetology

**Sensitivity and Specificity of the Hemoglobin A1c Test in Predicting Type 2 Diabetes in Youth**

Although the hemoglobin A1c (HbA1c) test serves as a useful predictor of diabetes in adults, its sensitivity and specificity for predicting type 2 diabetes in youth is not well known. The aim of this study was to evaluate whether HbA1c maintains sensitivity and specificity, when compared to the oral glucose tolerance test (OGTT), in pediatric cases. Based on comparison of fasting plasma glucose (FPG) and OGTT two-hour plasma glucose (2-hr PG) levels to HbA1c test results, sensitivity and specificity of the HbA1c test in children was calculated using standard methods. The study group contained 48 individuals considered to be at risk for diabetes based on weight status (body mass index 85th %ile), preliminary glucose tests, or family history of type 2 diabetes. Of the 48 patients, 6 were diagnosed with diabetes or prediabetes based on FPG levels, 3 were diagnosed based on 2-hr PG levels, and 7 were diagnosed based on both FPG and 2-hr PG levels. Sensitivity of the HbA1c test was found to be 54% in reference to FPG levels and 90% in reference to 2-hr PG levels. Specificity of the HbA1c test was 80% and 86% in reference to FPG levels and 2-hr PG levels, respectively. The HbA1c test related more closely to 2-hr PG levels both linearly and in terms of test results, as seen in the sensitivity and specificity of the HbA1c test. In conclusion, HbA1c was not found to be a sensitive or specific screening tool for diagnosis of type 2 diabetes in youth.

**Intern:** Piiamaria Virtanen  
**Major:** Biology and Neuroscience  
**Mentor:** Homer L. Twigg III  
**Department:** Division of Pulmonary, Allergy, Critical Care, and Occupational Medicine

**Endothelial Monocyte-Activating Polypeptide-II Concentrations are Increased in Bronchoalveolar Lavage Fluid from HIV Positive Patients Who Smoke**

Endothelial monocyte-activating polypeptide-II (EMAP-II) is a pro-inflammatory and pro-apoptotic molecule that is linked to pathogenesis in emphysema. The incidence of emphysema is higher in HIV-infected subjects. Prior in vitro experiments have shown that HIV gp120 and cigarette smoke extract increase EMAP-II expression in lung endothelial cells. Thus we hypothesized that EMAP-II concentrations would be higher in bronchoalveolar lavage (BAL) fluid from HIV-infected subjects and smokers and that treatment of HIV infection would lower BAL EMAP-II levels. To address this hypothesis we used a commercially available ELISA to measure EMAP-II in BAL fluid from 30 HIV positive subjects before and one year after antiretroviral therapy and 10 normal volunteers. Initial experiments performed by spiking BAL with known quantities of recombinant EMAP-II demonstrated that BAL did not contain an inhibitory factor in the assay. In the HIV population cigarette smoking was associated with significantly increased EMAP-II concentrations in BAL at baseline and after one year of treatment. Antiretroviral treatment for one year did not change BAL EMAP-II concentrations. Subgroup analysis did not show an increased EMAP-II in patients with lower CD4 counts at baseline or poor virologic control at one year. Assays to measure EMAP-II in non-HIV subjects have been negative to date. These results are being confirmed in additional experiments. In conclusion, HIV positive subjects who are also exposed to cigarette smoking express significantly increased EMAP-II concentrations in BAL, which in turn could contribute to the elevated risk of emphysema in these subjects.
Semi-autonomous Collision Avoidance System in a Driving Simulator

In 2009, there were more than thirty million older drivers aged 65 years and older in the US, a 23% increase from 1999. More than 5,500 older adults died and more than 183,000 were injured in motor vehicle accidents in 2008. Age related declines in various areas of functioning including cognition, vision, hearing, and processing contribute to the increased safety risk for older drivers. New technology and driving assistance systems, such as the semi-autonomous collision avoidance system, have the potential to decrease this safety risk for older drivers. The goal of this study was to investigate participants trust and opinions of the semi-autonomous collision avoidance system. Additionally, the study also investigated the amount of crashes experienced by participants in both a baseline drive condition and with the semi-autonomous collision avoidance system. As a Life Health Sciences Intern at the Indiana University Occupational Therapy department, I participated in the study design, simulation creation, data entry, and the recruitment and consent of participants. Results of this study will contribute to the understanding and future design of driving assistance systems and their implications for older drivers.

The Function of Amot Dimerization in Lipid Binding

Amots are adaptor proteins which coordinate signaling for cellular differentiation and proliferation. Their ACCH domain binds lipids with specificity leading to membrane deformation. A critical feature of Amot proteins is a novel lipid-binding domain, the Amot coiled-coil homology (ACCH) domain, which has the ability to selectively bind monophosphorylated phosphatidylinositols (PI) as well as target transcription factors to the nucleus. Understanding the biophysical mechanisms involved in lipid binding may provide pathways to modulate protein sorting and downstream signaling events inducing cellular differentiation, cancer cell proliferation, and migration. The central hypothesis is that characterizing Amot lipid-binding events will enable specific modulation of Amot isozyme for the prevention of ductal cell hyperplasia progression into breast cancer tumors. Synthetic membranes are used to demonstrate the role of dimerization in the ability to maintain ACCH-lipid binding activity. The specific aims of this work are: 1) Delineate the properties of the ACCH domain that provide for a dimer switch; and 2). Define the lipid-interaction properties of the ACCH domain homo- and hetero-dimer.

Site-directed mutagenesis was employed to probe the specific contributions of 37 selected lysines and arginines. We first measured the mutation stability through DSF, and then for their ability to dimerize using DLS. We then compare that information with that garnered from intrinsic tyrosine absorbance to understand the changes in structural conformations as a function of the mutation and lipid binding. As a result, we look to provide further information about which conserved residues participate in dimerization as a mechanism to control hetero- and homo-dimer formation.
Streptococcus mutans is a bacterium commonly found in the oral cavity of humans and plays a primary role in the formation of dental caries (cavities). It is known that nicotine affects the growth of S. mutans. When in the bloodstream S. mutans binds to endothelial cells, possibly leading to atherosclerosis. In this experiment, three strains of S. mutans serotype k were exposed to various concentrations of nicotine to determine their binding to human endothelial cells. Strains 51, 52, and 89 of S. mutans serotype k (UA159) were incubated with eight different concentrations of nicotine (0, 0.25, 0.5, 1.0, 2.0, 4.0, 8.0 and 16.0 mg/mL) for 24 h, biotinylated, and left to set for at least 24 hours. The cells were then fixed with 0.5% formaldehyde and kept in a cold room until needed. The human endothelial cells (HVEC) were coated on nonsterile 96-well flat-bottom microtiter plates and 1% bovine albumin serum was used to block any sites the endothelial cells did not bind to. After being washed with tween saline, the biotinylated bacteria were added to all wells except for the control group. A 1:2000 dilution of extravidin HRP in tween saline was added and incubated for 1 hour and OPD was added to each well to produce a yellow color change. The amount of color change correlates to the amount of bacteria that bound to the endothelial cells. A greater color change directly correlated with greater binding. The amount of color change (the optical density) was quantified using a SpectraMax190 spectrophotometer. It was determined that nicotine increased the bacterial binding to endothelial cells up to 4 mg/mL. Concentrations of 8 and 16 mg/mL were too toxic for the bacteria to survive. The observations from this experiment could suggest an increased risk of atherosclerosis for smokers.

Pulmonary arterial hypertension (PAH) is characterized by marked proliferation of pulmonary arterioles, leading to increased pulmonary pressures and ultimately right ventricular (RV) failure and death. Previous studies have shown that sex differences, including estrogen levels, can affect pulmonary vascular remodeling and disease prognosis. However, the specific contribution of endogenous sex hormones in PAH-induced pulmonary vascular and (RV) remodeling are not well known. Male and female Sprague-Dawley rats (175-200g, n=4/group) received sugen (Su5416; a VEGF receptor 2 antagonist) followed by 3 weeks of hypoxia (Patm=362 mmHg) and 4 weeks of re-exposure to room air (Patm=760 mmHg). Selected females underwent ovariectomy (OVX) prior to SuHx-PAH induction, with one group of OVX animals undergoing 17beta-estradiol (E2) replacement (75 mcg/kg/d, via subcutaneous pellets). Experimental groups were as follows: (1) normoxia male control, (2) normoxia female control, (3) Su-Hx male, (4) Su-Hx female, (5) female Su-Hx OVX, and (6) female Su-Hx OVX treated with E2 pellets. Both male and female SuHx rats exhibited a higher degree of pulmonary vascular remodeling than their respective normoxia controls (50.75+/-.46) and (47.95+/-.57) respectively. Female SuHx OVX did not differ from female SuHx (52.84+/-.61). However, E2 replacement in SuHx OVX significantly decreased PA wall thickness (38.06+/-.19; not significant vs. female normoxia 27.93+/-.19). RV fibrosis increased in both female and male SuHx groups (3.27+/-.73 and 4.81+/-.88, respectively). OVX did not alter fibrosis in female SuHx (4.69+/-.21). E2 administration to SuHx OVX further increased RV fibrosis.
Intern: Sarah Torline  
Major: Psychology

Mentor: Mary Ott  
Department: Adolescent Medicine

Teens Having the Capacity to Consent to Research (THINCCR): A Trial Study

The ability to consent to research is one of the most important ethical components of research. With adolescents, there is a lack of any one type of psychometric design to access whether or not they can be potential research participants. This is partly due to the great dissimilarity in individual differences; such as IQ and cognitive abilities. Through developing a psychometric measure that appropriately increases adolescents understanding of different types of consent, the more adolescents can become able participants in research. In a structured qualitative interview, young people between the ages of 12—24 years were chosen to answer a short survey asking demographic information and to read aloud a list from the Rapid Estimate of Adult Literacy in Medicine (REALM survey). Then, they listened to a few simulated studies that were about a clinical trial for migraine medicine, an STD screening, and a bio bank study. Participants were asked randomly throughout the consent a series of questions accessing there competence, understanding, reasoning, and appreciation of the consent forms. The different types of assessment tools used to score the answers were the MacArthur Competence Assessment Tool (MacCat-CR), the Brief Assessment of Capacity to Consent (UBACC), and the Evaluation to Sign Consent (ESC). The scores from the MacCAT-CR were correlated with the other measures to see if it did improve the adolescents understanding of the different types of consent. The results from this study will help future research in trying to create a standardized tool for adolescents to consent to research.

Intern: Garret Hillsdon-Smith  
Major: Biology and Chemistry

Mentor: Hiromi Tanaka  
Department: Molecular Genetics

Detection of Human Telomerase in Plasma: A Potential Simple Blood Test for Cancer Diagnosis

Telomerase is a unique ribonucleoprotein enzyme that maintains chromosomal telomere length. Telomerase activity has been shown to be very low or absent in human non-malignant somatic cells, however, is activated in nearly 90% of human cancers. Therefore, telomerase has been proposed to be a useful diagnostic marker for cancer. In this study, we investigated whether the presence of cancer correlates with telomerase activity in the corresponding plasma, thus representing a surrogate serological maker for cancer patients. Plasma telomerase activity was measured by the TRAP (Telomeric Repeat Amplification Protocol) assay in 5 patients with colon cancer, 6 patients with breast cancer, and 7 in healthy control subjects. The TRAP is a PCR-based method and takes only a few hours to obtain the results. Our preliminary data show a trend that telomerase activity in plasma distinguishes between healthy subjects and cancer patients. Thus, our finding provides an idea that a useful blood test for cancer diagnosis may be developed using the TRAP assay in plasma. Further case-control studies are necessary to assess the current outcome.
Osteoclast-Autonomous Defect Due to pG213R Mutation in the Clcn7 Gene Leads to Human ADO2 Disease in 129 Mice: New Insights into Treatments

ADO2 is a heritable osteosclerotic disorder that usually results from heterozygous missense mutations in the chloride channel 7 (CLCN7) gene. This disease is characterized by a wide range of symptoms and severity including multiple fractures, and is presently incurable. To understand the pathogenesis of this disease, we developed mouse model of ADO2 on 129 background. Compared to wild-type (WT), heterozygous (HT) ADO2 mice showed significantly higher (p<0.05) whole body aBMD and BMC. Trabecular bone at distal femur analyzed by CT revealed that HT mice had significantly higher (p<0.005) BV/TV, Tb.N, Tb. Th but lower Tb.Sp compared to WT mice. Serum biochemistry analysis indicated that calcium and phosphorus level did not differ between WT and HT mice, however, serum CTX/TRAP5b ratio was lower in HT mice compared to WT littermates. In concert with ADO2 patients, bone marrow cells from these ADO2 mice, cultured with M-CSF and RANKL, showed increase osteoclast (OC) formation, larger OC size and smaller resorption pits, confirming cell autonomous impairment of bone resorption. Gene expression analysis using OC from these mice showed that Cak, Csf1 and Dcstamp expression were lower but Tnfrs11a and Calca expression was higher in the HT mice. Administration of VitD3 in the ADO2 mice did not rescue their bone phenotypes while treating the OC from the HT mice with an inhibitor of apoptosis (IAP) antagonist increased their resorption. This mouse model will help us to identify the cellular and molecular basis of human ADO2, and to test innovative therapies to treat this incurable disease.

A longitudinal evaluation of the spatial concordance in location of visual field defects

Primary open-angle glaucoma is a chronic and progressive eye disease in which the loss of retinal ganglion cells leads to losses in visual function. If left untreated glaucoma can lead to permanent blindness. Glaucomatous damage usually occurs in one eye before it appears in the other. A previous cross-sectional study showed that approximately 35% of abnormal visual field locations in one eye were also abnormal in the other eye. The purpose of this project was to determine whether inter-eye concordance would increase over time. We included 29 patients with at least 5 visits and selected a reference visual field in the eye in which glaucoma was most advanced. The reference visual field had a repeatable defect that included a cluster of at least three points. We predicted that there would be an increase in inter-eye concordance as the severity of the defect in the non-reference eye increased. We compared the reference visual field to each consecutive visual fields in the non-reference eye. The concordance ratio was calculated using this formula, 2C/(A+B+2C), where “C” represents points that were abnormal in both eyes, “A” represents points that were abnormal in the right eye only, and “B” represents points that were abnormal in the left eye only. On average, the inter-eye concordance ratio did not increase over time. In some patients, an increase in the inter-eye concordance ratio was observed over time. Further research is needed to determine mechanisms that determine the location of visual field defect between the eyes as glaucoma progresses.
**Effects of compounds on endothelial cells and ocular cancer cells**

Retinopathy of prematurity (ROP) and wet age related macular degeneration (AMD) are caused by excessive growth of abnormal blood vessels in the eye and are leading causes of vision loss in the world. Although drugs exist to block this abnormal angiogenesis, these are expensive and not effective in all patients, so novel therapies are needed. We hypothesize that compounds that show inhibitory effects on primary human retinal microvascular endothelial cells (HRECs), and do not show such effect on ocular cancer cells can be used as an efficient drug leads to stop ocular neoangiogenesis without damaging other ocular cell types. In this study, the main focus was to test the effect of several compounds on three different cell lines: 92-1, a uveal melanoma cell line; Y79, a retinal cancer (retinoblastoma) cell line; and HRECs,. The compounds that were tested in this study are novel analogs of a natural compound that has shown antiangiogenic effects. In order to do this study, first cells were grown in 96 well plates and then different dilutions of compounds were added to the cells. The effect of the compounds was studied by measuring the number of cells after a 48 hour incubation with compound, using a florescent readout called alamarblue that assays the concentration of living cells in a sample. The four compounds that were tested on endothelial cells have shown inhibitory effects. Three of the same compounds did not show any inhibitory effect or had very low inhibitory effect in high concentration of compound when tested with 92-1 and Y79 cell lines (GI50 above 200 µM). In conclusion, according to our hypothesis these three compounds could be efficient drug leads to prevent ocular neoangiogenesis.

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**Alveolar Proliferation and Apoptosis Levels in Mouse Emphysema Following hASC Treatments**

Chronic Obstructive Pulmonary Disease (COPD) is a progressive disease that causes difficulty in breathing due to loss of elasticity and destruction of airways and air sacs. COPD is the currently the third leading cause of death in the United States, and is largely caused by cigarette smoking. Airway damage in mice with emphysema is seen in the form of enlarged airspace and increased alveolar cell apoptosis and proliferation turnover. We hypothesized that intraperitoneal (i.p.) or intravenous (i.v.) human adipose tissue-derived stem cell (hASC) treatments after cigarette smoke exposure would show significant alveolar repair through a decrease in apoptosis and alveolar space, and possible increase in proliferation. Male and female NSG mice were exposed to cigarette smoke (CS) or ambient air (AC) for a period of 6 months. After 6 months, exposure to CS was stopped and subgroups were given hASC cells once a week via i.v. or i.p. for an additional 2 months. The lungs were harvested, and paraffin sections were used to perform immunohistochemistry using several antibodies for proliferation (Ki67 and Cyclin D1) and apoptosis (Caspase-3, Bcl2/Bax, and TUNEL assay). CS caused a decrease in Caspase-3 and an increase in the Bcl2/Bax ratio. hASC (i.v.) treatments caused an increase in Ki67 and Cyclin D1, as well as an increase in Caspase-3 and TUNEL, and a decreased Bcl-2/Bax ratio compared to CS-exposed animals. These results indicate that hASC caused an increase in proliferation, but also presented higher apoptosis levels post-treatment in the lungs of CS-exposed mice.
Structure and Mechanics of Primate Prehensile Tail Vertebrae

Prehensile tails (PTs)—capable of suspending the body weight of the animal—evolved independently as many as 14 times among 40 extant mammalian genera. The structure of the mammalian PT is well studied in New World monkeys, where it evolved twice: once in the atelines and once in the genus Cebus. Adult PTs share musculoskeletal features that distinguish them from nonprehensile tails, which are thought to be adaptive to the mechanical demands of suspension and/or prehension incurred with locomotion, posture, and manipulation: 1) craniocaudally expanded sacroiliac joint and more proximal region vertebrae; 2) more expansive transverse and hemal processes (proximal and distal attachments for primary tail flexors, respectively); and 3) tail vertebrae that are estimated to be structurally stronger and more rigid. Yet, our understanding of the broader adaptive significance of the PT has been hampered by two major deficits. First, structural data are largely limited to cortical and trabecular geometric assessments, which only provide estimates of mechanical properties and therefore limit the mechanical conclusions we can draw. Second, our studies have concentrated solely on the features of the adults even though we know anecdotally that tail-use behavior changes ontogenetically. Therefore we expect that these changes are reflected in the mechanical properties of the tail vertebrae. The present study demonstrates that cortical geometric assessments correlate with structural mechanical properties of tail vertebrae in an ontogenetic series of squirrel monkeys, and both sets of data reveal a trend of increasing structural strength of the vertebrae with increasing body size (i.e., age).

Effects of Thrombopoietin (TPO) on Longitudinal Mouse Hind Limb Crush Injury Model

Approximately 645 people suffer from blunt force trauma injury to the femur every day. The recovery time of such injury can last anywhere from 3-6 months. Thrombopoietin (TPO) was used as a growth factor to induce bone and muscle healing. In this study, nine separate mouse groups (10 mice per group) were used: Crush PBS, Crush TPO, Surgery PBS, and Surgery TPO at day 3 and day 17, and controls with no surgery/crush/treatment. Skeletal muscle was harvested from the following sites: experimental impact, experimental adjacent, and normal contralateral skeletal muscle as a control. The muscles were fixed, processed, sectioned, and stained with H&E and Massons Trichrome stains. The slides were reviewed for skeletal muscle injury, muscle necrosis, inflammation, muscle atrophy, and muscle regeneration. Additionally, F4/80, an immunostain for macrophages was performed. On microscopic examination at day 3 the most common histologic changes seen were sporadic muscle fiber vacuolation, focal necrosis of varying sizes, muscle contraction bands, and infiltration of macrophages. On day 17, the skeletal muscle injury was generally healed. The main histologic lesions seen were variable sizes of muscle fibers, early fibroplasia, fat infiltration, some macrophages, satellite cells, and neovascularization. Comparing the TPO treated mice versus the PBS control group, the lesions at both time points were less in the TPO treated mice.
Apps Enabling Public Transportation

The purpose of this study was to review literature pertaining to computer apps that are in development or currently available for the use of people with disabilities in order to use public transportation systems. Even though new technologies have been developed to support community mobility, many people are still unable to travel in the community. This lack of community mobility can lead to social isolation, decreased quality of life, and inability to participate in desired and required occupations. 1) What applications can be used by people with disabilities to assist with transportation? 2) What entities exist to track developments in transportation apps? A narrative review of the literature was conducted, by searching sixteen relevant databases. Term combinations used were based on three categories: terms relating to community mobility, terms relating to disability, and terms relating to technology. Research was conducted in six phases starting with the broadest search using the Boolean operator “OR” and then narrowing down the Boolean operator “AND”. Articles were selected based on consensus using inclusionary and exclusionary criteria. Ancestral searches were then conducted on the first set of materials. In the ancestral search articles cited in the original material were located and materials were selected based on consensus using inclusionary and exclusionary criteria. The original database searches resulted in 147 references that where then summarized, along with 73 ancestral references. From the summaries themes where identified in the categories of devices, communication, accessibility, navigation, users, and systems.

Effect of Kalirin Domains on Alkaline Phosphatase Activity in Osteoblasts

Osteoblasts (OBs) are important for maintaining bone formation. Disruption between the balance of OBs and osteoclasts, which are responsible for bone resorption, can lead to osteoporosis, a disease that causes a decrease in bone density and an increase in bone fragility. Disruption of the function of OBs can also lead to low bone mass. Our lab has previously published that Kalirin, a GTP-exchange factor protein, is important for regulating bone mass. Global deletion of Kalirin in mice results in osteoporosis. Kalirin plays a role in the signaling pathways of OB function, but its mechanism of action is unknown. There are three different isoforms of Kalirin: Kal7, Kal9, and Kal12. Each of the isoforms contain different functioning domains that may have an effect on the function of OBs. To further study the relationship between Kalirin and OB function, the effects of different Kalirin protein domains on the activity of alkaline phosphatase (ALP), an enzyme responsible for osteogenic activity, were examined in an osteoblast cell line, MC3T3-E1. Constructs of Kalirin were made which contained four protein domains: GEF1, GEF2, IGFN and Ser/Thr kinase. MC3T3-E1 cells were transfected with these Kalirin constructs and ALP assays were then performed on the cells. The experiments revealed that GEF2 leads to an increase in ALP activity, while the Kinase, GEF1 and IGFN domains have no distinguishable effects on ALP activity. In conclusion, since Kalirin is known to activate RhoGTPase via its GEF domains, the GEF2 domain may be increasing ALP activity by increasing Rho activity in OBs. Identifying ways to activate GEF2 may be a novel target to increase bone regeneration, which can then be applied for the treatment of bone loss associated with periodontal disease and osteoporosis.
**LIFE-HEALTH SCIENCES INTERNSHIPS**

**Intern:** Mai Khuu  
**Major:** Biology  
**Mentor:** Ann Kimble-Hill  
**Department:** Biochemistry & Molecular Biology

Toward understanding the role of Amot130 lipid binding in cellular proliferation and migration

Amots are adaptor proteins which coordinate signaling that controls cellular differentiation and proliferation. Amot proteins have a novel lipid binding domain, the Amot coiled-coil homology (ACCH) domain, which selectively binds monophosphorylated phosphatidylinositols (PI) and targets transcription factors to the nucleus. Understanding the biophysical mechanisms of lipid binding may provide pathways to modulate protein sorting and downstream signaling events inducing cellular differentiation, cancer cell proliferation, and migration. So far, all work reported on signaling based on Amot expression fails to distinguish between the role of the Amot80 and the 130 family members as they share a common ACCH domain. The goal of this project is to specifically associate the Amot130 ACCH lipid binding with function related to ductal hyperplasia and breast cancer phenotypes. Mutations were carried forward based on lipid sedimentation, FRET, and SAXS assays against the ACCH domain. Site-directed mutagenesis was employed to probe the specific contributions of 7 selected lysines and arginines toward lipid head-group binding in the full length protein. Target proteins will be fluoresced to determine whether they retain their ability of binding to membrane. Cells fractionation will be used to quantify the protein amount that has passed the nuclear membrane. Amot family members bind core polarity proteins controlling the apical domain organization of epithelial cells; and Yap, a transcriptional co-activator that regulates cell growth. Mutations in Amot affecting lipid binding to the apical membrane lead to disability to control cell growth and differentiation. Consequently, abnormal phenotypic changes regarding cell migration and polarization will be observed when growing cells on matrigel assays.

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**Intern:** Heather Reeves  
**Major:** Philosophy  
**Mentor:** Zeynep Salih  
**Department:** Pediatrics, Riley Hospital for Children

Training for Delivering Difficult News Using Simulation: Results from a Pilot Project in a NICU Setting

Each year, 10-15% of babies born in the U.S. are admitted to the Neonatal Intensive Care Unit (NICU). It is imperative for physicians to learn how to communicate effectively and empathetically to help parents in this situation. However, a recent study concluded that the majority of physicians lacked the communication skills and knowledge of how to deliver difficult news. The aim of this pilot project was to test the feasibility and perceived effectiveness of communication training using SPIKES, Ask-Tell-Ask, and NURSE protocols in the NICU setting. The communication training sessions were held in-situ in a level II NICU. Participants consisted of medical students and pediatric med/peds residents. Sessions lasted approximately 60-70 minutes and focused on the case of a mother who had given birth to a baby with the possible diagnosis of Down’s Syndrome (T21). The intern acted as a standardized patient, specifically as the young mother who portrayed different reactions to the difficult news being delivered. Before each simulation, participants received a short, interactive information session about basic communication skills and examples for Ask-Tell-Ask and NURSE. Following the simulation, participants completed a survey to articulate their overall impression of the session and judge its effectiveness. In both sessions, the medical students and residents reported the communication training sessions were relevant to NICU situations and the session helped develop their skills in delivering difficult news. The researchers are encouraged with the initial results and plan to continue the sessions using professional actors and to study and process the patient outcomes.
Characterization of grooming behaviors in Outbred P-rats as a TTM/DTM model

Trichotillomania (TTM) and Dermatotillomania (DTM) are body focused repetitive diseases (hair pulling and skin picking) affecting as much as 4% of the population causing impairment in daily function and significant distress. Women are 4 times more likely to be affected than men. The diagnostic criteria for TTM have been detailed in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), but DTM is not as well described. The inbred C57Bl/6 mouse displays clinical signs and behavioral characteristics similar to those described for women suffering from these diseases. A behavioral test was developed to identify predictive responses that indicate a mouse will develop clinical signs, making this mouse a potential model of these diseases. Because alcohol preferring P-rats also display the clinical signs and behavioral characteristics, we hypothesized that this outbred stock could be a more valuable animal model. In this study, 172 female p-rats were recorded on digital media for 15 minutes after being sprayed with a mist of water and assessed for grooming patterns—oral, manual and scratching. Oral grooming showed significance (p=0.0078) as a predictor of which animals would develop skin lesions. This study suggests that P-rats may be a preferred model to study TTM and DTM due to the outbred rats increasing genetic variation which mirrors human population affected by TTM/DTM. The results of this pilot project will allow us to seek funding from NIMH/NIH regarding future studies of intervention modalities for Trichotillomania and Dermatillomania.

Analyzing the level of activity (both in-patient and out-patient visits) of different research areas of the CRC in 2013

The Indiana Clinical and Translational Sciences Institute (CTSI) is one of 60 CTSAs funded by the National Institutes of Health. These CTSAs facilitate laboratory (translational) research into clinical trials in a shorter time frame. This process aids in developing new treatments faster and enhancing the field of translational research. The Clinical Research Center (CRC) is part of the CTSI and provides space and nursing support to conduct academic and industry-sponsored clinical research studies for both inpatient and outpatient visits. The CRC conducts both adult and pediatric protocols in several disciplines including; Anesthesia, cardiology, dermatology, endocrinology, diabetes, gastroenterology, general internal medicine, gynecology, oncology, hematology, infectious diseases, genetics, nephrology, neurology, obstetrics and gynecology, pathology, rheumatology, pharmacology, psychology, psychiatry, radiology, speech and hearing services, and surgery. The purpose of this project was to analyze the level of activity (both in-patient and out-patient visits) of different research areas in 2013. The number of patient visits for each discipline was obtained from Web CAMP (the software program used for CRC data collection), and the percentages were calculated to determine proportional relationships among disciplines.
**Intern:** Alexa Lahren  
**Major:** Nursing  
**Mentor:** Mary Ott  
**Department:** Adolescent Medicine

_**Teens Having Capacity to Consent to Research**_

Informed consent is a critical aspect of health care decision-making and safe participation in research. Adults are assumed to have capacity and small children to not have capacity, but less is known about adolescent capacity to consent. Adapting an adult tool for adolescents, this study examines adolescent capacity to consent to health care research in three areas: epidemiologic research, a biobank, and a randomized controlled trial. I have conducted semi-structured interviews with adolescents, using the Macarthur competency assessment tool for clinical research (MacCAT-CR) to assess their ability to give informed consent, and administered a questionnaire to assess factors, such as age, health literacy, and health status, to evaluate variables that might influence informed consent. This information gives the tools required to create consent processes that are tailored to adolescents’ capacity, making research and clinical trials safer and more accessible.

**Intern:** Jaymin Patel  
**Major:** Biology  
**Mentor:** David P. Basile  
**Department:** Department of Cellular and Integrative Physiology

_Acute kidney injury transition to chronic disease induced by high salt diet is associated with Th-17 cell differentiation and is dependent on Ang II signaling_

Recovery from acute kidney injury (AKI) by ischemia-reperfusion (I/R) coupled with a high salt diet in Sprague-Dawley (SD) rats creates an efficient model for studying chronic kidney disease (CKD). Developing research suggests that the immune system hastens the progression from AKI to CKD. Therefore, a study was performed to characterize lymphocyte activity during this transition. Male SD rats were subjected to unilateral I/R injury and recovery. At 5 weeks, rats sustained unilateral nephrectomy (UNX) leaving either the injured (direct/ipsilateral) or uninjured (remote/contralateral) kidney and were subsequently exposed to elevated dietary NaCl (4.0%) for an additional 4 weeks. Rats with a solitary injured kidney showed evidence of increased albuminuria and interstitial fibrosis following transition to a high salt diet. To examine the potential role of Ang II signaling on lymphocyte differentiation in this model, post-I/R rats were treated with the AT1 antagonist losartan (30 mg/kg/day in drinking water) just prior to the UNX and high salt treatment (i.e. at 5 weeks). Losartan resulted in 80% reduction in the number of Th-17 cells at 9 weeks post I/R relative to untreated injured controls (P<0.05). Similarly, losartan tended to reduce the levels albuminuria and interstitial fibrosis relative to the untreated control I/R rats. Taken together, these results suggest that high salt diet triggers the activation and differentiation of pro-inflammatory Th17 cells following recovery from a prior ischemic injury and that differentiation is dependent either directly or indirectly by AT1 receptor.
Observing trends in Prescription Drug Abuse within Marion County

Prescription drugs have become a major role-player within American society today. The functions and side effects of these medications have led to both their abuse and overuse. Considering this, a report from the Trust for America’s Health was released in October of 2013 with the purpose of highlighting the growing trends in these misuses. This study was done to take a glimpse at the misuse of these medications within Marion County, and compare it to the data found within the above report. For this research, 6 years (from 2007 to 2012) of death records were compiled from the Indianapolis Marion County Coroner’s Office. In these records, it was determined that a total of 716 drug overdose deaths occurred over the 6 year period. However, this total does not offer a delineation of the various types of drugs involved in these overdoses. Delving further, it was determined that 421 of these deaths can be attributed, at least in part, to prescription medication drug use from the years of 2009 to 2012 (there was no clear separation of the drugs involved in the death records for 2007 and 2008). In conclusion, it was determined that the growth rate over the six-year period (2007 to 2012) of this study was similar (about 280% increase compared to the 12 year (1999-2010) determination for the entire state of Indiana of 350% increase) to the previous report’s findings for the state of Indiana.

Investigation Of A Novel Countermeasure Against Acute Radiation Syndrome

Detonation of an improvised nuclear device (IND) would result in the exposure of individuals to doses of ionizing radiation (IR) that would cause a spectrum of symptoms collectively known as the acute radiation syndrome (ARS). There is no effective treatment for ARS; thus, new and innovative research is required to develop timely and efficient radiation countermeasures that can be administered after exposure to IR, whether they be pharmacological or non-pharmacological. In the human, ARS may occur in individuals receiving doses of 1-15 Gy. It is possible to combat some of the effects of doses of ~3 to ~9 Gy through hospitalization and the limited drug countermeasures currently available. Wild-type C57BL/6 mice provide an excellent model for studying radiation countermeasures in humans. Our lab has found “protective wounding” to be a highly effective strategy for increasing the survival of male and female mice which have received total-body exposures of ionizing radiation. “Protective wounding” involves the creation of a small subcutaneous incision midway down the dorsal surface after irradiation. The mechanism behind “protective wounding” was explored through the analysis of complete blood counts (CBCs) from blood collected through non-lethal tail bleeds. Serum was also collected and analyzed for cytokines that might be involved in the protective response. While our data have yet to reveal the mechanism of “protective wounding”, further studies of the cytokine profiles of wounded mice may prove useful in determining this mechanism, and the development of an effective pharmacological countermeasure.
The purpose of this study is to investigate how adolescents’ beliefs about the consequences of smoking are affected by their level of emotion regulation, with negative urgency (NUR) as a moderator variable. “Negative urgency,” a facet of impulsivity, refers to the tendency for certain individuals to engage in rash actions as a result of negative affect (Cyders & Smith, 2008). The study consisted of 60 nicotine-naive youth, between the ages of 10 and 14.9, with varying degrees of genetic and phenotypic risk for the development of substance use disorders. The participants completed the UPPS-P, a questionnaire measuring impulsivity (including negative urgency) (Whiteside & Lynam, 2001), and the Smoking Consequences Questionnaire (Lewis-Esquerre, Rodrigue, & Kahler, 2005) and a parent completed the Emotion Regulation Checklist (Shields & Cicchetti, 1997) about their child. It was hypothesized that lower emotion regulation would predict positive expectations about the consequences of smoking, with negative urgency as a moderator. There was a significant correlation (p=.004) between emotion regulation and beliefs about smoking consequences in individuals with high levels of negative urgency (NUR +1SD, NUR = -1.42). In other words, at high levels of negative urgency, poor emotion regulation has a significant effect on smoking beliefs. This suggests that negative urgency may be especially important in influencing the onset of risky behaviors such as smoking.

Pulmonary arterial hypertension (PAH) is a progressive disease that causes increased resistance in the small to mid-size pulmonary arteries. Elevated pulmonary pressure increases the work of the right heart and can lead to right ventricular (RV) hypertrophy and failure, and ultimately to death. No cure currently exists for PAH; however exercise has been shown to reduce some of the symptoms associated with PAH. Patients with PAH exhibit an increased right ventricular systolic pressure (RVSP). Using a monocrotaline-rat model of PAH, our lab recently demonstrated that rats that completed a 45 minute treadmill run at moderate intensity had lower RVSP compared to unexercised counterparts. Since RVSP was measured immediately following exercise, it was hypothesized that the lower RVSP in the exercised group was due to an acute exercise-induced stimulation of pulmonary vasodilation, and not to diminished arterial wall thickness. To confirm this, formalin-agarose filled and paraffin-embedded lung tissue was sectioned and stained for smooth muscle actin (alpha-SMA), a protein found in the contractile unit of smooth muscle which surround blood vessels, using standard immunofluorescence (IF) technique. Thickness of the smooth muscle actin-stained wall of the pulmonary arteries was compared between exercise and un-exercised PAH and healthy rats. While PAH rats exhibited pronounced pulmonary vessel muscularization as expected, there was no significant difference in wall thickness for acutely-exercised PAH rats, compared to non-exercised PAH rats. Subsequent experiments in our lab verified that the decreased RVSP in acutely exercised PAH rats was likely due to an increased activation of pulmonary endothelial nitric oxide synthase (e-NOS) and increased production of the potent vasodilator nitric oxide.
The Luminal Progenitor Compartment of the Normal Human Mammary Gland Constitutes a Unique Site of Telomere Dysfunction

Telomeres are essential in the upkeep and regulation of the genome, but little is known about their regulation of the normal human mammary gland. There is now a cell population that is phenotypically defined as having many luminal progenitors, characterized by unusually short telomeres. The length of these telomeres is not related to donor age. It has also been found that multiple DNA damage response proteins colocalize with telomeres in 95% of luminal progenitors but in 5% of basal cells. That may be partially explained by the fact that only luminal progenitors have increased telomerase activity. Interestingly, this potential telomere repair mechanism declines with age. The experimental findings reveal differences in telomeres of four different subsets of cells: basal epithelial cells, luminal progenitor cells, mature luminal mammary tissue, and nonepithelial stromal cells. The cells were isolated at a high purity (95%) and were analyzed for telomere length by quantitative phosphorimage scanning of telomere restriction fragment (TRF) lengths in southern blots and quantitative PCR. The strange telomeres of the luminal progenitors may have potentially important implications for certain breast cancer development.

Analysis of didelphid marsupial prehensile tails: functional specializations in terrestrial and arboreal species

Bone geometry and architecture has been shown to vary across taxa with different behaviors, as bone tissue responds by adapting to differences in mechanical loading. In primates and procyonids (raccoons and relatives), prehensile tails—ones that are capable of suspending the entire body weight of the animal—have vertebrae with larger cross-sectional properties (estimates of bending and torsional strength and rigidity) than those in nonprehensile tails. This has not been examined in other taxa. In this study, we examined 6 different species in the Didelphidae family (oppossums and relatives) that are grouped in two groups, arboreal and terrestrial. The 3 species within each group vary in mass such as: small, medium, and large. Both groups have prehensile tails but we hypothesize that the opposing functions will lead to different bone structure and strengths. Micro-CT scanning of 5 functionally analogous caudal vertebrae allowed us to measure various aspects of bone geometry and architecture, including cross-sectional cortical properties and trabecular shape (SMI). Purely using measurements of the scanned specimen, we were able to estimate bone geometry, density, and strength. It was seen in the Longest Vertebrae, that there was significant difference between groups and within groups as well. The arboreal group data shows direct relation between body mass and bone geometry, density, and estimated strength. On the other hand, the terrestrial group only shows relation between body mass and estimated bone strength. The explanation of these results can be linked to the known uses of the tails of in each group or species itself.
Type II Diabetes Mellitus

Diabetes Mellitus affects nearly 25 million in the United States and 100 million people worldwide. Diabetes is characterized by increased blood glucose beyond the physiological range. It develops when the body does not produce enough insulin to maintain normal glucose level or when cells do not respond to insulin. Type 2 diabetes mellitus (T2DM) or insulin dependent diabetes is the most common form. Measuring fasting and postprandial glucose in blood samples obtained by finger stick is commonly used for monitoring diabetes. This is painful and ineffective in long-term diabetics due to poor circulation. Furthermore, by the time abnormal glucose regulation is identified, the underlying pathological process has progressed for many years. Hence there is need for identifying biomarkers for early identification of T2DM.

Increased circulating cytokines and adipokines released by the fat tissue are reported in T2DM. Saliva and serum share large number of proteins. Hence we hypothesized that the assessment of T2DM associated cytokines, adipokines and insulin related proteins in saliva could provide a non-invasive method to identify potential markers for diabetes. Unstimulated whole saliva was collected from T2DM patients reporting to the clinics of the Indiana University School of Dentistry after obtaining informed consent. Salivary TNF-&alpha;, IL-6, ghrelin, visfatin, and resistin was determined by enzyme-linked immunosorbent assay (ELISA). The concentration of TNF-&alpha; was significantly lower and that of IL-6 and visfatin was significantly higher in the saliva of diabetes subjects as compared to that of healthy controls. Our observations suggest that these proteins could represent potential biomarkers for T2DM.

TGFβ1 is sufficient for cushion formation of mouse embryonic heart

Defect in valve formation is a potential cause of congenital heart disease. Increased TGFβ1 has been reported in Loey-Dietz syndrome-afflicted adults with congenital heart defects and valve malformations. Cardiac cushions, precursors of valves and septa, are formed by epithelial-mesenchymal transition (EMT). Tgfβ1 is expressed during EMT in the cardiac tissue of normal mice. Tgfβ1-/- mice have no cardiac defects, suggesting that TGF&beta;1 is not required for heart development. Conditional overexpression of active TGFβ1 in endocardial cells was used to determine if Tgfβ1 overexpression alters cardiac cushion formation. Analysis of histologically stained serial sections indicated severe cardiac malformations in the Tgfβ1 conditional transgenic embryos. Analysis of total cushion area and cushion cell count showed enhanced cushion formation in Tgfβ1 conditional transgenic embryos compared to control embryos. Immunohistochemistry analysis of Ki-67 - a marker of cell proliferation - indicated that enlarged endocardial cushions in Tgfβ1 transgenic embryos were not caused by increased cell proliferation, suggesting that cushion formation was increased in the Tgfβ1 conditional transgenic mouse embryos. These results indicate that TGFβ1 alone is sufficient for cushion formation in the mouse embryonic heart.