IUPUI Life-Health Sciences Internship Program

Spring 2012 Poster Session and
Fifth Year Celebration

Friday, April 13, 2012
3:00 PM—5:00 PM
VanNuys Medical Science Building Atrium
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.

Welcome to the IUPUI Life-Health Sciences Internship Program Spring 2012 Poster Session and Fifth Year Celebration.

This year the Life-Health Sciences Internship Program celebrates five years of connecting 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.

Life-Health Sciences Internship students represent 27 different majors and minors 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, the Indiana University School of Nursing, Methodist Research Labs, and the pharmacy department of Indiana University hospital (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

The IUPUI Life-Health Sciences Internship Program is funded by the Indiana University Commitment to Excellence Grant.
Thank you to our 2011-2012 participants:

Interns

Andrew Alexander  Ashutosh Kale
Mohammad Aref     Shelby Kale
Damilola Awonusi   Lindsey Keener
Cory J. Banaschak  Kelsey Lipking
Shelby Blasingame  Gabriel Martinez
Anna Brenneman     Haley McGough
Jon Carnahan       Callie Meece
Paige Conroy       Diana May Natividad
Morgan Deno        Anh Nguyen
Alyssa Elliott     Binal Pandya
Sarah Flores       Jamie Parker
Aiza Garcia        Emily Potts
Rachel Gardner     Kevin Pritchard
Kirian Gill        Austin Reilly
Rachel Giordano    Kendra Rode
Kristen Grothaus   Mohamad Salkagi
Hayley Grzych      Neelam Shah
Iraj Hassan        Marina Sharif
Katharine Havard   Kimberly Smith
Alicia Herb        Alison Spahr
Sean Hiett         Floyd Timm
Mallory Huser      Evan Torline
Sara Ibrahim       Rhea White
Vibhuti Jani       Shalin Zia
Benjamin Judge     Shameem Zia

Intern: Shameem Zia
Major: Biology
Mentor: Janna Hilligoss
Department: Rheumatology

NOVEL USE OF KETOTIFEN (MAST CELL STABILIZER) IN FIBROMYALGIA: A PILOT STUDY

Our proposal seeks to test the feasibility of a treatment trial using ketotifen (mast cell stabilizer). In this trial, we conduct a 10-week randomized placebo-controlled trial to determine the effects and to estimate the effect sizes of ketotifen on three outcome measures: fibromyalgia (FM)-related pain severity, blood chemokines (i.e., IL-8, MCP-1 and eotaxin) and pressure pain threshold. We hypothesize that ketotifen will have greater beneficial effects than placebo in reducing the severity of FM-related pain and the levels of blood chemokines and lowering sensitivity to pressure stimuli. This pilot study is the first to investigate the effects of an immune-based therapy on FM-related pain, and also the first to evaluate chemokines as biomarkers of disease severity. This innovative research is expected to impact human health in two ways: (1) pave the way for a large clinical trial to test the efficacy of ketotifen as an adjunctive therapy for the management of FM; and (2) provide a scientific foundation supporting the development of other intervention strategies that targets chemokines and/or mast cells.
Characterizing Risk of Type I Diabetes (T1D) in Relatives of Persons with T1D

Type 1 diabetes is a disease that results from the destruction of pancreatic \( \beta \)-cells. Although all people are susceptible, relatives with T1D are at much greater risk for development of the disease. The study that I assisted with during my internship is an international, NIH-funded multicenter research project called the T1D TrialNet Pathway to Prevention (PTP) Study. PTP is designed to examine how T1D develops in at-risk individuals with an eventual goal of intervening to change the natural history of the disease. The study starts by persons who have a first or second degree relative with T1D undergoing a screening blood test to look for the presence of autoantibodies as markers of higher risk of developing T1D. When patients screen positive for one or more autoantibodies, they then are asked to return for a confirmatory blood test. We found that many persons (46%) who had screened positive did not return for confirmatory screening. As part of my internship, in addition to helping contact patients who need to schedule visits, I have been looking at why participants did not schedule follow-up visits for confirmatory labs. I sent out letters and short surveys to participants who did not follow up with to obtain answers in order to better improve our study in the future. Once we have data from these surveys, we will query the national coordinating center to see if the reasons why persons did not return for screening here in Indiana are similar to those that lead to non-returns internationally.
Intern: Andrew Alexander  
Major: Psychology  
Mentor: Dr. Mary Ott  
Department: School of Medicine Adolescent Section

Challenges/Solutions to Community-Based Research with Adolescent Boys

Purpose: Little research has been conducted about the sexual health of 14-17 year old adolescent males. This study examined the sexual health of adolescent males from poor socioeconomic backgrounds within this age range using a venue-based research design in order to gain insight specifically on males who are unlikely to go to a clinic for treatment.

Methods: A total of 667 adolescent males, aged 14-17, were recruited for this study. Participants were asked to take a 15-20 minute survey on an iPad; which covered their sexual health, relationships, and the participant's sexual activity. Upon completion of the survey, subjects were asked to supply urine samples for a DNA-based STI-test which detected the presence of Trichomonas, Gonorrhea, and Chlamydia. The participant was then given a $20 gift card for taking part in the study. Urine samples were taken to a lab and processed. Results: A number of participants tested positive for STIs; 3.7% were positive for Chlamydia while less than 1% tested positive for Gonorrhea (0.6%). Our sample was ethnically diverse with 48.7% of participants being African American, 36.3% European American, 8.4% were Asian or mixed race, and 6.4% identified as Hispanic. Conclusion: Our findings suggest that the sexual health of adolescent males is an area which warrants attention and intervention due to STI rates being extremely high for this age demographic. One important finding was that adolescent males are interested in receiving information about their sexual health from a trusted adult.

Intern: Rhea White  
Major: Social Work  
Mentor: Patricia J Scott, PhD, MPH, OT  
Department: Occupational Therapy

PANCREAS/KIDNEY TRANSPLANTATION: COPING RESPONSES

Transplantation in persons with Type 1 diabetes, with simultaneous kidney transplantation or alone, typically follows many years of deteriorating health, dialysis to compensate for lack of kidney function and often disability income for economic support. Despite a careful pre-transplant screening, the transplant team at IU Health University Hospital has observed that some individuals thrive and rapidly return to successful independent living, and others struggle, presenting with a myriad of dependencies, and emotional and social problems. Given the scarcity of organs for transplantation and the significant resource allocated to individuals who receive transplants, it is critical to assure we are supporting the recipients of these scarce organs. Therefore understanding of the factors which are associated with these positive and negative outcomes will allow the transplant team to develop approaches to improve patient care. One concern is that habits to maintain health needed before transplant, if not redirected to productive habits, have been shown to remain after transplant. This research takes a systematic approach to the identification of pre-transplant factors associated with this differential coping response. Through this research we are hopeful to identify pre-transplant indicators that predict post-transplant adaptive capacity such that we can better prepare individuals to successfully cope following transplant and return to full productive lives.
Comparing the Rate of Parasitic Infection Among People of Rigores, Honduras to Guatemala

Honduras is the second poorest country in Central America, and thousands of its residents are living without access to medical care. Parasites are an everyday reality there, and rates are more than double that of Guatemala. The Honduras ENLACE Project at Indiana University School of Medicine Department of Family Medicine sends medical brigades to Rigores, Honduras to help combat this. The Department of Family Medicine wants to know why Honduras has such high rates of parasites compared to its neighbor of Guatemala. This research analyzes the data from the March 2011 brigade and compares it to national health data from Guatemala. Problems common to Honduras were reflected in the data and were not surprising. These included diabetes, hypertension, malnutrition, and parasitic infections. Specifically, comparisons showed people living in Guatemala have lower rates of parasites. It was found that Guatemala has much higher numbers of improved drinking water sources as well as improved sanitation systems, which were directly related to the lower rates of parasites. The data collected and analyzed from Rigores compared to that of Guatemala may help future brigade teams help decrease the parasitic infection rate.

Assessing the bone anabolic properties of a traditional medicinal compound

Osteoporosis is a common bone disease that increases the risk of bone fracture. Current osteoporosis medications are targeted towards either inhibiting bone resorption (antiresorptive agents), or stimulating bone formation (anabolic agents). The use of parathyroid hormone (PTH), the only currently FDA approved anabolic therapy, is limited because of its cost and duration limit (2 years). Therefore, the need for other anabolic agents exists. The goal of this study is to investigate the anabolic properties of a traditional medicinal compound (BENS, Bone Enhancing Nutritional Supplement) used in several countries to treat bone fractures and osteoporosis. To accomplish this goal, this pilot study utilized a rat model of post-menopausal osteoporosis to investigate the skeletal properties of BENS as compared to PTH. Ovariectomized animals were treated daily with vehicle (VEH), low or high doses of BENS, or PTH. After 4 weeks of treatment, bones were analyzed using micro-CT (to assess bone architecture) and histomorphometry (to assess bone formation rate). Compared to VEH-treated animals, PTH increased trabecular bone formation rate (+90%), while BENS produced an intermediate effect (+39% and +46%, respectively compared to VEH). On cortical periosteal surfaces, low dose BENS resulted in higher bone formation compared to both VEH and PTH. These preliminary results suggest that BENS has potential as a bone anabolic therapy and warrants further study.
**Racial differences in Intra-Ocular Pressure and Central Corneal Thickness in people with healthy eyes**

**Purpose:** Previous studies show conflicting results as to the existence of racial differences in intra-ocular pressure (IOP). Some studies report higher IOP in people of African descent (AD) compared to people of European descent (ED), while other studies show no differences. Central corneal thickness (CCT) can affect IOP measurements, with thinner corneas leading to lower IOP measurements. Several studies have shown that people of AD have thinner CCT. The goal of this study was to determine whether racial differences in IOP exist in people with healthy eyes and whether these differences can be explained by differences in CCT.

**Methods:** IOP and CCT were measured in people with healthy eyes (N=13). Of the 13 participants, 8 (62%) were of AD and 5 (38%) were of ED. The IOP was measured using Goldman applanation tonometry. CCT was determined by taking the average of three measurements using an ultrasonic corneal pachymeter. The following factors were also recorded: age, blood pressure, and heart rate. T-tests were used to compare the data from the AD and ED groups.

**Results:** No statistically significant differences were observed in IOP, CCT, age and heart rate between the AD and ED groups (p>0.05). There was a significant difference in systolic heart rate (p=0.049), but no significant difference in diastolic heart rate between the AD & ED groups (p=0.53).

**Conclusions:** These results suggest that people of AD and ED with healthy eyes have similar intra-ocular pressures and central corneal thickness.
Assessment of DNA Isolation Methods from Human Tissue for Optimal Yield and Purity

The placenta is a temporary organ that develops during pregnancy that serves as a barrier between fetus and mother as well as a place for nutrients to pass through to the fetus. Genomic imprinting deals with the expressed allele of the two inherited genes, the other being silenced. Through single nucleotide polymorphisms (SNP), we can determine whether the imprinted allele came from the maternal or paternal side. Also, the quality of DNA is important when genotyping to determine the genetic make-up of the individual. The long term goal of this research study is to see how the effects of intrauterine exposure to adverse conditions can affect imprinted gene expression in placental tissue and how these changes can lead to future health risks. We used various methods for DNA isolation from placental tissue including a QiaAmp Mini Kit (Qiagen) as well as a TRIzol reagent (Ambion). The object of my project was to compare the various DNA isolation methods to how they rated on their yield, their DNA purity, and whether they resulted in PCR inhibition.

A Comparison of Cell Permeability Between Linear Peptoids and Their Triazine-Bridged Cyclic Peptoids Counterparts

The goal of this project is to evaluate the cell permeability of triazine-bridged cyclic peptoids in comparison with their linear counterpart. The triazine-bridged cyclic peptoids, recently developed by this group, should have a significantly higher level of conformational rigidity than the general linear peptoids. The rigidity enables them to bind to a target protein with high affinity and/or high selectivity, giving them notable interest in medical research. When compared to native peptides, the linear peptoids are generally much more cell permeable. This project will systematically examine if the cyclic peptoids demonstrate a similar level of permeability as their linear counterparts. A series of cyclic and linear peptoids were synthesized with fluorescence labeling. Their cell permeability was then evaluated by using FACS and fluorescence microscopy to observe their interactions with the cellular membrane.
Study of Teamwork through Video Recordings of In-situ High Fidelity Simulations in a Level IIIC NICU

Simulation is a tool used for training and educational purposes. We conducted realistic in-situ high fidelity simulation sessions at Riley Hospital’s Neonatal Intensive Care Unit (NICU) using a SimNewB (Laerdal, Inc.) baby in a patient care unit. Nurses, respiratory therapists, fellows, and nurse practitioners participated in the simulations, which imitated several resuscitation scenarios. After the scenario was completed, the simulation group participated in a debriefing. There were two simulation sessions and two debriefings in the first round. There will be another simulation session and debriefing about 3 months later. All simulations and debriefings were video recorded. The purpose of this research is to assess the feasibility of using video recordings to score teamwork. Along with other interns, I actively participated in setting up the video equipment and the simulation room. I also observed the simulation sessions as well as the debriefings. Once all simulation sessions were completed I began to analyze the video recordings. We used the State Obstetric and Pediatric Research Collaboration (STORC) Clinical Teamwork Scale to develop a scoring technique for the simulations. Key phrases and actions are noted under the specific category on the Clinical Teamwork Scale to fit the model of the NICU. We are in the process of finalizing the nature of scoring the videos. Once completed, we will train outside scorers to score the simulation sessions. Results thus far have illustrated that it is possible to use video recordings to score teamwork in the NICU.

Telomere fusions in early human breast carcinoma

Several lines of evidence suggest that defects in telomere maintenance play a significant role in the initiation of genomic instability during carcinogenesis. While the general concept of defective telomere maintenance initiating genomic instability has been acknowledged, there remains a critical gap in direct evidence that telomere dysfunction occurs in human solid tumors. To address this topic, we devised a multiplex PCR-based assay [TAR (telomere associated repeat) Fusion PCR] to detect and analyze chromosome end-to-end associations (telomere fusions) within human breast tumor tissue. Using TAR Fusion PCR, we found that human breast lesions, but not normal breast tissues from healthy volunteers, contained telomere fusions. Telomere fusions were detected at similar frequencies during the early ductal carcinoma in situ (DCIS) stage and the later invasive ductal carcinoma stage. Our results provide direct evidence that telomere fusions are present in human breast tumor tissue and suggest that telomere dysfunction may be a critical driving component sparking genomic instability. Development of this robust method that allows identification of these genetic aberrations, telomere fusions, is therefore anticipated to be a valuable tool for dissecting mechanisms of telomere dysfunction and detecting early forms of breast cancer and potentially other solid tumor types.
Intraoperative Neuromonitoring and Anesthetic Fade with Total Intravenous Anesthesia (TIVA): Final Data Report

The purpose of this study is to investigate the effect of total intravenous anesthesia (TIVA) on intraoperative neuromonitoring (IONM) during spinal surgeries; specifically the monitoring of motor evoked potentials and somatosensory evoked potentials (SSEPs). Factors being assessed include: if anesthetic fade occurred or not, and if surgical recall was experienced. IONM is used in high risk surgeries that put the nervous system at risk to prevent post-operative deficits (observed negative changes in the patient after surgery). Forty-five patients undergoing spinal surgeries were selected for this study. The recording of MEPs were made bilaterally from the abductor pollicis brevis/abductor digiti minimi (hand), tibialis anterior (shin), gastrocnemius (calf), abductor hallucis/adductor digiti minimi (foot). The amplitude of each compound muscle action potential (CMAP) from each muscle group was recorded at half hour intervals for each case. The recording of MEPs were made bilaterally from the abductor pollicis brevis/abductor digiti minimi (hand), tibialis anterior (shin), gastrocnemius (calf), abductor hallucis/adductor digiti minimi (foot). The amplitude of each compound muscle action potential (CMAP) from each muscle group was recorded at half hour intervals for each case. All of the cases used were surgeries that lasted more than 5 hours. The research presented will be used to confirm the reliability of using TIVA and demonstrate the benefits of it over general anesthesia for IONM and MEPs.
**INDIANA BIOBANK**

With today’s growing medical advances in technology, the realm of what research can explore is endless. In order to conduct research, scientists need a wide variety of samples. The Indiana Biobank provides researchers with a resource that combines a blood bank and patient health information all in one place. This is done in efforts to increase gains in Hoosier health by allowing specific genetic factors in health and disease to be studied and accessed. The biobank allows the researcher easy access to blood samples that is specific to what health phenomena is being researched. By going to the Biobank, researchers can request samples of blood that can be refined by gender, age, current medications, diseases present and the list continues. In order for the biobank to offer its resources to researchers, several steps have to be accomplished in order for the biorepository to function optimally. In the simplest terms, the actions of the biobank can be broken down into four main categories: 1. Collection kit production; 2. Recruitment and consenting; 3. Specimen collection; and 4. Laboratory processing. The Indiana Biobank works in conjunction with ResNet, a primary care practice-based research network that provides research assistants to recruit for the biobank. The Indiana Biobank team, researchers, collaborators, clinics and hospitals and most importantly the communities are integral to the biobank’s success in making it a useful and beneficial tool in research advances.

**The Rho-GEF Kalirin Regulates Bone Length in Female Mice**

During growth, bone remodeling results in the progressive lengthening of bones and an increase in bone mass, until peak bone mass is reached. Kalirin is a novel GTP-exchange factor protein and we found that deletion of the kalirin gene in mice (Kal-KO) leads to a 41% decrease in the bone mass of female mice at 14 weeks of age, compared to a 20% decrease for male mice. In this study, we examined the length of bones from wild-type (WT) and Kal-KO mice to determine the potential role of kalirin on longitudinal bone growth. We collected tibia from WT and Kal-KO female and male mice at 14 weeks of age, removed associated muscle tissue and then used a digital caliper to measure bone length. The average length ± SD was recorded and a student t-test was performed. The tibia from female WT and Kal-KO mice were found to be 18.04±1.04 mm (n=9) and 16.99±1.06 mm (n=16) in length, respectively. The tibia from male WT and Kal-KO mice had an average length of 18.17±0.53 mm (n=15) and 17.79±0.70 mm (n=16), respectively. These studies reveal that the tibia of female WT mice are significantly shorter than tibia from female Kal-KO mice (p=0.013). In contrast, the tibia of male Kal-KO mice are not significantly shorter than the WT mice (p=0.052), although they approached statistical significance. These studies suggest that Kalirin is involved in regulating bone length in female mice, suggesting it may play a role in the development of the skeleton during growth.
INCIDENCE AND EVALUATION OF CATATONIC SYMPTOMS IN A STATE PSYCHIATRIC HOSPITAL

One of the most intriguing and under-studied areas of psychosis is catatonia, a debilitating neuropsychiatric condition. It is often recognized when a patient presents with extreme negativism (resistance towards attempts to move a person) or catatonic excitement (excessive, purposeless motor activity). Since Kahlbaum's discovery of it in 1874, many attempts have been made to specifically characterize the symptoms of catatonia. The syndrome itself can be divided into four main categories: negativism/withdrawal (mutism, staring, stupor, catalepsy), automatism (inability to refuse commands, waxy flexibility), repetition/echoing (perseveration, verbigeration, echopraxia, echolalia), and agitated/resistive (resistance to instruction, contrary behavior, combativeness, impulsivity, psychomotor agitation). Based upon these symptoms, work has been done to produce clinical rating scales in order to recognize catatonia in patients with other or subtler presentations & standardize assessment of catatonic symptoms. Without using catatonia rating scales, only 1.3% of psychiatric inpatients have been diagnosed with catatonia. On the other hand, using catatonia rating scales, recent studies have shown that 18% of subjects have exhibited two or more catatonic signs. Given the prevalence of the symptoms and degree of impairment which they confer, further efforts should be directed at diagnosis and assessing these symptoms. The primary aims of this study is to further this aim by determining the prevalence of catatonic symptoms in patients suffering from psychotic illness and comparing two scales for the assessment of catatonic symptoms, the Busch Francis Catatonia Rating Scale (BFCRS) & screen (BFCS) and the KANNER (Katatonia Autism Neuropsychiatric and Neuromovement Examination Rating).

Study of Staff Perceptions After Interdisciplinary High-fidelity In-situ Simulations in a Neonatal Intensive Care Unit

This study is part of a bigger project titled “Improving Teamwork During Neonatal Resuscitation: Linking Training Using Simulation, Personal Social Networks, and Larger Clinical Culture” in which we are aiming to find out the perceptions of the participating staff toward simulation sessions held in the Riley Children's Hospital Neonatal Intensive Care Unit (NICU). We worked with teams of nurses, respiratory therapists, and pediatric residents using a high-fidelity simulator (SimNewB, Laerdal, Inc.) in a room set up to resemble the actual NICU module, where the teams practiced neonatal code scenarios. Immediately after each scenario, we took the participating team members to a separate room adjacent to the NICU for an interdisciplinary structured debriefing session. After two consecutive sessions and debriefings, participating staff were given a survey that asked about their perceptions of the quality and usefulness of the simulation sessions. A majority of the staff found the sessions beneficial in terms of improving their communication and teamwork skills, and they asked for more sessions.
Comparison of Ehlers-Danlos Syndrome with Rheumatoid Arthritis and Lupus

Many genetic disorders present symptoms that are very similar to other syndromes and other diseases. Ehlers-Danlos Syndrome (EDS) is a heritable disorder that causes a defect in an individual’s connective tissues. The symptoms of EDS are often caused by faulty collagen. Collagen is a protein that helps to add strength and elasticity to the body’s connective tissue. Rheumatoid Arthritis (RA) and Lupus are rheumatic diseases that manifest similar symptoms as the Classic and Hypermobility Types of EDS. In the Medical Genetics Clinic this year, several patients were seen that were referred by rheumatologist and primary care physicians for EDS after no rheumatic cause could be identified for their symptoms. These patients presented similar features as a RA patient or a Lupus patient would, but did not have positive blood work results to confirm either one of these diseases. While the exact gene(s) for RA and Lupus have yet to be identified, there have been several that have been linked to these two diseases. The objective of this research was to compare EDS with RA and Lupus. The diagnosis, symptoms, and treatment options for all three were analyzed to find any similarities. Then, the genetics of EDS, RA, and Lupus were researched and examined to see if there was any correlation between the three. While there were similar findings in the symptoms and even treatment/management options for all three, there was not a strong correlation between genes and their locations to make the assumption that all three are some how related.

Novel Use of Oral Ketotifen for the Treatment of Fibromyalgia

Fibromyalgia is a condition that involves chronic pain throughout the entire body and has a profound impact on the lives of the 2% - 4% of the population that it affects. The pain associated with fibromyalgia is caused by an increased number of mast cells in the body that release histamines, which causes inflammation and pain. There are not many effective drugs available for fibromyalgia patients, and there is no definitive diagnosis, cure, or treatment. In this ongoing investigational new drug study, Ketotifen, a mast cell stabilizer (antihistamine), will be used in order to determine the effects it has on three aspects related to fibromyalgia: pain severity, chemokines in the blood, and the threshold of pressure and pain. This new drug study will continue for a ten week duration and involves randomizing volunteers into one of two groups: one group will receive the active dose of medication, and the other group will receive a placebo. From this pilot study, we hope to determine if the drug Ketotifen is effective in reducing the symptoms of fibromyalgia. If we do find it to be effective, a larger study will be designed based on the same principles as this pilot study. The purpose of this possible larger study would be to provide a definitive diagnosis for fibromyalgia by looking at specific blood markers present in fibromyalgia patients, and also to provide a new drug that is effective in reducing the symptoms associated with fibromyalgia.
Nicotinamide therapy retards the growth of ectopic calcifications in a murine model of familial tumoral calcinosis

Patients with mutations in the GALNT3 gene suffer from tumoral calcinosis, characterized by often large, ectopic calcific masses in soft tissues, due to persistent hyperphosphatemia. Surgical removal of the calcific mass is the most common treatment of the condition, but in most patients, calcific mass will recur, requiring a more permanent solution to the problem. In this study, we investigated nicotinamide as a potential therapy for tumoral calcinosis, using a murine model of the disease - Galnt3 knockout mice. First, an appropriate dose of nicotinamide necessary to lower blood phosphate levels was determined by testing a range of doses (0, 2.5, 5, 7.5, and 10 mmol/kg/day; oral) over two weeks in normal mice. Subsequently, the effect of nicotinamide was tested in Galnt3 knockout mice on a high phosphate diet. After four weeks on the high phosphate diet, some of the mice developed ectopic calcifications. At that point, high-dose nicotinamide mixed in water treatment (dose 10 mmol/kg; oral) was given over four weeks. The radiographic data pre- and post-treatment showed that nicotinamide did not clear the calcification, but retarded its growth, while in the untreated, calcifications increased in size significantly. The collected data indicate that nicotinamide over four weeks may not completely remove ectopic calcifications, but show promise for longer treatments or possibly higher dose treatments.

Group OT for Fall Prevention after Stroke (GOT falls?)

Many Americans each year sustain a stroke. In fact, strokes are considered the most disabling chronic disease in the US and are associated with many health risks. Among these health risks include numerous threats to the individual’s independence and safety. Such vulnerabilities include various levels of disability and an increased fall risk. This single arm, 6 week group Occupational Therapy intervention provided fall risk education for people with stroke and focused on how to prevent and manage fall risk as well as increase falls self-efficacy. The participants consisted of 10 male veterans with an average age of 64. Of these, 70% were white and were on average 34 months post stroke. The intervention was based on an existing, effective group OT fall prevention program which we tailored to people with stroke. The intervention was taught by an occupational therapist in two hour sessions each week. Identification of fall risks, prevention strategies, and proper safety techniques were communicated and shared amongst the veterans. We used the Falls Self-Efficacy scale to assess falls self-efficacy and the Falls Control scale to assess perceived control of fall risk and the Falls Prevention Strategies & Survey to assess fall prevention strategy. All were assessed pre and post intervention and analyzed. Significant and nearly significant improvements were found post-study in the Falls Control (p=0.046) and Falls Prevention Strategies & Survey (p=0.064) scales. Our findings suggest a positive association between fall risk factor education and perceived control in fall risk.
**TRPV1 Channels in Dog Coronary Artery Smooth Muscle Cells**

Capsaicin is the active component of chili peppers and is considered to be beneficial for cardiovascular health because it dilates coronary arteries through an endothelial-dependent mechanism and may slow atheroma progression. We compared the effects of capsaicin on coronary arteries isolated from dogs versus pigs. We investigated whether there is any species difference in the sensitivity to capsaicin. We first performed isometric tension experiments using freshly isolated dog coronary artery rings. We found that capsaicin induced a biphasic response, with transient endothelial-dependent dilation following by sustained contractions in dog coronary arteries. In contrast, pig coronary arteries exhibited only capsaicin-induced dilations. We then isolated smooth muscle cells (SMCs) from adjacent dog coronary artery segments and by using a fluorescence imaging approach, confirmed that capsaicin stimulated intracellular Ca2+ rises in a population of dog coronary artery SMCs. Using a specific TRPV1 inhibitor, we demonstrated that capsaicin acts on TRPV1 channels in dog coronary artery SMCs. We propose that capsaicin may cause coronary vasospasm in dog coronary arteries.

**Driving Simulation**

The privilege to drive has a myriad of benefits to people of all ages, especially in The United States where public transportation may be lacking or problematic for individuals who do not live in a large city or who may have disabilities. In an effort to enable drivers of varying abilities to achieve a greater level of independence in their lives, assistive technology has been researched and applied to road vehicles. After using a battery of cognitive and physical assessments, in conjunction with a high fidelity driving simulator, a comparison of these tasks was made between approximately sixty subjects in order to assess the relationship of performance between various ages and abilities. As a result of this research, it has been shown that within the stratified age groups, there was minimal variability except for the sixty-five and older group. In comparison between the rest of the subjects, this group exemplified lower Useful Field of View scores which corresponded to their driving behaviors. In conclusion, there is evidence from multiple cognitive and physical tests that assist in the determination of a driver's ability to function in different roadway conditions. Some of the implications may lie under the difficulties of motion sickness due to using a simulator. However, it can also be determined that such a sequence of related tests is beneficial in determining a driver's current abilities.
**Getting the Word Out: IUSM Office of Public and Media Relations and Indiana CTSI**

The IU School of Medicine Office of Public and Media Relations delivers a variety of news releases about noteworthy research at the IU School of Medicine, upcoming events, grants and funding, and a variety of other topics in research and development. The stories and events are broadcast through Scope, the IU School of Medicine Newsletter, MedTV, a closed-circuit TV system used for broadcasting events and announcements, and Sound Medicine, a public radio talk show where medical experts are interviewed on a wide range of current issues.

Some of the stories remain internal, others are delivered to the public—including the School of Medicine, the IUPUI Campus, and a few are even released on a broader scope (the Indianapolis Star, the National Science Foundation, and the Huffington Post, for example).

The Indiana Clinical and Translational Science Institute (CTSI) is a statewide collaboration of Indiana University, Purdue University, and the University of Notre Dame, which encourages translation of scientific discoveries in the lab into clinical trials and new patient treatments. The IU main location is found at the Health Information and Translational Services (HITS) building. Indiana CTSI provides different types of grants and levels of funding for researchers and scientists, financially assisting them in all stages of research. The clinically-certified laboratory facilities can also accelerate the traditionally slow research process. CTSI also releases news stories about funded researchers and their projects on their website (indianactsi.org) as well as in an online and print newsletter.

**Building the Type 1 Diabetes Exchange Registry Database**

Type 1 diabetes (T1D) is an autoimmune disease which is increasing in prevalence. Yet, many persons with T1D have poor disease management. Improving treatment of this complex, chronic disease is essential for ensuring the comfort and safety of the individual. As there are numerous factors contributing to an individual’s blood glucose control, including insulin dosing, accounting for carbohydrates eaten, and adjusting dosing for exercise and illness, management of this disease can be extremely difficult. Recognizing the need for advancement in understanding, the T1D Exchange was founded. Initiated in September of 2010, the initiative involves investigators and patients at 67 adult and pediatric centers across the nation. One of the Exchange goals is to develop a national registry in which data from patients with diabetes is collected and then examined. As of the end of March, there were just under 24,000 patients enrolled in the database.

Recruitment into the Registry involves giving consent/assent and then, using an iPAD, providing survey information about topics ranging from demographics and degree of blood sugar control to insulin delivery plans to the frequency and type of glucose monitoring. The hopes are to use these data to improve the treatment methods and identify the most effective methods of management of T1D. Riley Hospital for Children is participating in the recruitment of T1D patients for this study. At this site alone, approximately 700 patients have agreed to become part of the database. I have worked during the internship to enroll patients in diabetes clinics.
**Effec of Caffeine on Streptococcus mutans**

**Planktonic Growth, Biofilm formation and Metabolic Activity**

Streptococcus mutans is the main bacterial cause of dental caries, and it has been shown in previous research that its growth is affected by various levels of nicotine and other agents. The concentration of S. mutans is directly proportional to the number of dental caries in the mouth. Research in our lab and others has been shown that smokers have increased dental caries due to the nicotine being a promoting agent for S. mutans growth. Due to dental plaque bacteria being introduced into the bloodstream, S. mutans has also been proven as a cause of cardiovascular disease. It has been observed that many people while smoking, are drinking some particular caffeinated beverage, usually coffee. Previous research has determined that coffee reduces dental caries as it interferes with S. mutans ability to adhere to the tooth surface. Although research on the effects of caffeine on S. mutans is not completely clear, it has been suspected that caffeine is an inhibitor of S. mutans. The objective of this research was to observe how caffeine affects S. mutans planktonic and biofilm growth and biofilm metabolic activity. The planktonic growth curves of S. mutans were studied using various concentrations of caffeine as well as studying the effects of caffeine on S. mutans biofilm formation and metabolic activity. These experiments concluded with results proving that caffeine acts as an inhibitor of S. mutans. The amount of caffeine in one cup of coffee, 6 mg/ml, significantly retards planktonic growth, and inhibits biofilm formation. The higher concentrations of caffeine inhibit S. mutans more effectively than the lower concentrations (.075 mg/ml). However, even at the lowest concentration of caffeine used, S. mutans growth was significantly inhibited. These results provide evidence for the inhibitory effect of caffeine on S. mutans biofilm and may indicate a mechanism for the effect coffee has on reduction of caries.
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**DMAPT as a Potential Radiosensitizer for Pancreatic Cancer Cells**

Pancreatic cancer is the fourth leading cause of cancer-related death in the United States with an estimated 37,390 deaths expected to occur in 2012. The prognosis is very poor due to the recurrence and metastasis of the cancer with a 6% five-year survival rate for all stages combined. This study examined the effectiveness of dimethylamino-parthenolide (DMAPT) as a radiosensitizer to the human pancreatic cancer PaCa2 cell line. It is hypothesized that DMAPT, a bioavailable drug derived from parthenolide, will inhibit the activation of NF-kappaB and enhance radiation-induced cell killing of PaCa2 cells. NF-kappaB is a transcription factor that promotes cell survival, tumor progression, and angiogenesis and reduces susceptibility to apoptosis. The results show that DMAPT was toxic to the PaCa2 cell line. As a result, DMAPT suppressed cell growth and increased the doubling time of PaCa2 cells. The combination of 4μM DMAPT and radiation decreased cell survival. The PaCa2 cell line is radiosensitized by DMAPT but further investigation is required to determine the mechanism through which DMAPT works.
Does research published in mainstream journals represent the priorities of children worldwide?

Background: The Millennium Development Goals (MDGs) created by the World Health Organization (WHO) are long-term goals targeted towards a variety of epidemics affecting the globe. MDG4 aims to reach a 2/3 reduction in mortality of children <5 years old by 2015. Deaths <5 have been linked to six conditions: neonatal, pneumonia, diarrhea, malaria, measles, and HIV/AIDS. Currently, it is unclear how much the mainstream medical and pediatric community are informed with or interested in MDG4.

Objective: To evaluate the number of publications related to the MDG4’s most frequent conditions in 7 major medical and pediatrics journals in the year 2010.

Methods: Using OVID we searched articles with keywords of: AIDS, HIV, diarrhea, malaria, malnutrition, measles, mortality, neonatal, pneumonia, and vaccination in Archives of Pediatric and Adolescent Medicine, BMJ, JAMA, Journal of Pediatrics, NEJM, and Pediatrics. Results: A total of 357455 hits were obtained; 440 abstracts were retrieved after applying limitations to MDG4, English Language, and eliminating duplicates. This constitutes 0.123% of all the publications in the 7 journals. The percentages of the topics covered are as follows: neonatal 104(0.029%), HIV 34 (0.010%), AIDS 9(0.003%), pneumonia 20 (0.006%), vaccination 42(0.012%), malaria 16(0.004%), measles 7 (0.002%), diarrhea 30(0.008%), malnutrition 17(0.005%), and mortality 161(0.045%). Only 52 (0.015%) were from clinical trials.

Conclusions: Although global health initiatives have been on the rise, only a small fraction of the research on MDG4 that has been published in popular medical journals reflects the current interest of the medical community in the most important goals impacting children worldwide.
The Influence of an Indiana Background on Practice Location Choice of Residency and Fellowship Graduates

As a result of a shortage of physicians in Indiana, the Indiana University School of Medicine (IUSM) and other residency programs must find ways to help meet the medical needs of the state. However, little is known about what influences residency and fellowship graduates’ choice to practice in Indiana. This study examines the association between Indiana connections and the graduates’ choice to remain in Indiana to practice. The Graduate Medical Education Exit Survey measured the graduates’ plans after graduation, intended location of practice, and reasons for their choices. Overall, 52.8% of graduates indicated they intended to practice in Indiana. Of the four measured connections graduates had to Indiana (hometown, high school, college, and medical school), 80.6% of graduates of IUSM were most likely to practice in Indiana. Analysis of the combinations of the graduates’ possible Indiana connections found that those who had a hometown and graduated from an IUSM were most likely to practice in Indiana (82.1%). This study also explored two reasons for practicing in Indiana, proximity to family and proximity to spouse/partner’s family. Those who graduated from an Indiana high school and college were mostly likely to stay in Indiana to be closer to family (73.0%). Those with a hometown, high school, and college in Indiana were most likely to stay in Indiana to be closer to their spouse’s or partner’s family (47.1%). These findings show that admitting graduates with connections to Indiana may increase the proportion of graduates who practice in Indiana.

Staining of OvCa1 Antibody in Human Malignancies

Immunohistochemistry biomarkers are being developed to target specific proteins found in cancer cells. The biomarker tumor suppressor, OvCa1, has not been well characterized. We developed monoclonal antibodies of OvCa1 to examine multiple human malignancies. Primary cancers with different histologic grades as well as metastatic lesions were examined with the monoclonal antibodies. Ovarian cancer tissue samples from the IU Simon Cancer Center Tissue Bank were used for this study. The samples were fixed in neutral buffered formalin and processed into a paraffin block. The slides were microtomed, and immunohistochemistry (IHC) with the OvCa1 antibody was performed. Thirty-one low, medium, and high grade tumors and metastatic ovarian carcinomas were evaluated. All cases revealed a range of staining intensity with OvCa1. The results indicated that OvCa1 had the highest immunostaining in the high grade, Stage 3 to 4 ovarian carcinomas. Medium grade tumors had less OvCa1 expression, while the metastatic tumors had less staining than any of the other three grades. Immunostaining was observed primarily in the cytoplasm and nucleus of the tumor cells. In addition, we evaluated approximately 20 tumors from various different organs. These included prostate, breast, spleen, lung, colon, stomach, and kidney tumors, which were positive for immunostaining with the antibody. In summary, the results indicate that all grades express the biomarker, OvCa1, and the staining intensity was highest in the high grade tumors. Our preliminary studies demonstrate a further need to delineate OvCa1 as a biomarker, which could be used for early detection and diagnosis of ovarian cancer.
An Anti-Acrolein Treatment Reduces the Expression of the Monocyte Chemoattractant Protein-1 in Nociceptive Neurons

Chronic pain is a frequent complication that follows spinal cord injury (SCI) in both clinical and animal studies. Oxidative stress due to the production of acrolein, an AB-unsaturated aldehyde, may contribute to SCI-associated pain behavior and the production of pro-nociceptive proteins including the chemokine monocyte chemoattractant protein-1 (MCP1; also known as CCL2) which plays a critical role in chronic pain facilitation via its binding to CCR2 receptors. Our goal in this project was to determine the degree to which spinal cord contusion induces expression of MCP1 in primary afferent nociceptive neurons in lumbar dorsal root ganglia (DRG). I first determined the degree to which SCI increases MCP1 in a population of non-peptidergic, nociceptive primary afferent neurons that bind the plant lectin, IB4. Immunolocalization of the chemokine in sensory neurons revealed that between 30-40% of the cells were positive for MCP1 (MCP1+) and over half of the MCP1+ cells exhibited the nociceptive neuron marker IB4. Hydralazine, a known acrolein scavenger, is known to reduce the incidence of chronic pain behavior following SCI. To this end, I determined the degree to which hydralazine treatment altered the percentage of cells that were MCP1+ and/or colocalized with IB4 in nociceptive neurons. These experiments revealed that while hydralazine only slightly diminished the percentage of injury-induced MCP1+ neurons, the treatment nearly eliminated the number of nociceptive neurons that were both MCP1+ and IB4 positive. Our data demonstrate that acrolein-mediated production of MCP1 may directly contribute to nociceptive signal processing in nociceptive sensory neurons.

Neuropathological approach for blast-wave induced mild traumatic brain injury

Veterans of Iraq and Afghanistan are extremely susceptible to complications derived from blast-wave induced mild traumatic brain injury (mTBI) sustained from road-side bombs and IEDs. Furthermore, there are 1.5 million civilian incidences of TBIs annually in the United States, and as many as 75% are considered mTBIs. mTBI is an important medical concern because 15% of patients can develop long-term cognitive, emotional, and behavioral problems from the initial injury. Often neuroimaging with traditional methods (CT or MRI) are usually negative; this is why mTBI has been coined the “invisible wound”. The pathological basis leading to the disorders are poorly understood, meaning there are no effective treatments for the neurological problems after the disorders have developed, making early and preventative care key. Using a blast-wave injury model, several mice were given injuries similar to those from the front lines. The damaged brains were collected, mounted, Golgi stained, and imaged at a high resolution to track the dendrite and spine degeneration. After quantification, it was found that even thought there was no lesion or dramatic cell death, the dendrites of the remaining neurons had become swollen and “beaded.” The mature “mushroom” spines, crucial for synapsis, suffered a 60% loss, and there was a roughly 30% loss in the overall number of spines. A widespread synaptic loss disrupts neural circuitry, contributing to neurological disorders. This experiment sheds light of the effect of mTBI, and suggests that neurodegeneration may be a novel target for developing diagnostic methods and therapeutic approaches for mTBI in the future.
Mdm2 in Bone Development and Osteoclastogenesis

Mdm2 is known to regulate the activity of p53 during early mouse development. Conditional knockout of Mdm2 in osteoblasts leads to skeletal defects. Clinically, gene amplification or elevated levels of Mdm2 are evident in osteosarcomas. To determine if we could generate osteosarcomas, the collagen 1.7 promoter, which is turned on in osteoblasts and osteocytes was ligated upstream of the Mdm2 cDNA and injected into embryos. Offspring from two founder lines were monitored for over 2 years with no evidence of osteosarcoma development at necropsy. Upon further analysis of female and male mice at various ages, it was evident that Mdm2 expression resulted in an increase in bone mineral density. Micro-computed tomography showed that Mdm2 expression resulted in an increase in cortical and trabecular bone formation in male and female mice. Histology showed a novel finding that during early long bone formation there was a massive increase in osteoclasts on the outside of the femur, suggesting that Mdm2 expression in osteoblast/osteocytes is resulting in osteoclast recruitment and reorganization of bone composition. To determine whether Mdm2-overexpressing osteoblasts facilitate osteoclast formation, we used a co-culture model system. Briefly, mature osteoblasts/osteocytes generated from the long bones of WT and Mdm2-overexpressing mice were co-cultured with osteoclast progenitors generated from WT and Mdm2-overexpressing mice. These studies demonstrated that Mdm2-overexpressing mature osteoblasts/osteocytes were capable of significantly enhancing osteoclastogenesis compared to littermate control cells. Taken together our results suggest that modest Mdm2 expression in mature osteoblasts/osteocytes positively influences bone formation and increases osteoclastogenesis without the induction of tumors.

Analysis of an FGF23 Gene Mutation in Tumoral Calcinosis

Iraj Hassan, Amie K. Gray, Leah R. Padgett, and Shoji Ichikawa Department of Medicine, Indiana University School of Medicine, Indianapolis, Indiana 46202 Fibroblast growth factor 23 (FGF23), produced mainly by osteocytes, regulates calcium, phosphate and vitamin D concentrations in the blood. Persistently low FGF23 concentrations due to mutations in either FGF23 or GALNT3 gene causes familial tumoral calcinosis, characterized by hyperphosphatemia and ectopic calcifications. A severely affected patient with tumoral calcinosis had compound heterozygous mutations in GALNT3, which are sufficient for disease manifestation. Interestingly, the patient had an additional nucleotide variation in the signal sequence of FGF23. To determine whether the variation is a mutation or polymorphism, <100 ethnicity-matched healthy controls were screened by Restriction Fragment Length Polymorphism (RFLP) analysis. None of the controls carried the FGF23 variation, suggesting that the mutation may affect localization of FGF23, contributing to the severity of the disease in the patient. To determine the functional consequence of the mutated gene, the coding sequence of wild type and mutant FGF23 was cloned into the expression vector, pIRES-hrGFP II. These clones were then expressed in HEK293 cells. The medium collected from the cells was used to measure FGF23 concentrations by enzyme-linked immunosorbent assay (ELISA). FGF23 concentrations from the cells expressing the wild type and mutant were not statistically different. Due to the lack of difference between wild-type and mutated FGF23, the gene mutation appears to have no effect on the FGF23 function and likely does not contribute to the severe manifestation of the disease in the patient.
A chart review on the effects of psychopharmalogical treatments on in-utero drug-exposed children

Children who have been exposed to drugs of abuse in utero are at an elevated risk for cognitive and emotional impairments and present with a higher risk of psychiatric abnormalities. In utero drug exposure may hamper the effectiveness of pharmacological treatment of these children, but little research has been conducted to guide treatment practices. This study focused on quantifying psychopharmacological treatment and its effects on children exposed to drugs in utero who are presenting for outpatient psychiatric care. We hypothesized that drug-exposed children would have a less positive response to medication and require more types of medication treatments than the psychiatrically ill non-exposed control group.

An IRB approved chart review identified data from 58 children (44 males) for this study - 30 children in the drug-exposed group, and 28 in the age-, sex- and psychiatric disorder-matched control group. Drug-exposed participants were selected based on their caregiver's report of in utero exposure to one or more drugs of abuse (opiates, benzodiazepines, tobacco, alcohol, marijuana, or stimulants). When compared using independent samples t-tests (p<0.05), there were no significant differences between groups in the number of medications children were on at arrival to the clinic (drug-exposed 1.40 +/- 1.248; control 1.07 +/- 1.152); in the number of medications prescribed throughout treatment at the clinic (drug-exposed 3.10 +/- 2.155; control 2.57 +/- 1.137); or in the number of medications prescribed upon leaving the clinic (drug-exposed 2.12 +/- 1.392; control 1.75 +/- .928). All participants improved over the course of treatment, with an average improvement in CGI score of 0.643 +/- 0.678 for the controls, and 0.333 +/- .606 for the drug-exposed group. These findings are not consistent with our hypothesis that the drug-exposed group would have a less favorable response to medication, as estimated by the number of prescribed medications.

Enhancement of Cytotoxic Effects of a Metalloenediyne by Hyperthermia on Pancreatic and Breast Cancer Cells

Enediynes are potent antibiotic DNA binding agents that induce damage upon the DNA double helix. These compounds have been evaluated as chemotherapeutic agents, but their cytotoxicity has limited their use in the clinic. Introducing metal ions within the enediyne skeleton can reduce the cytotoxic effects of the original compound. Interestingly, our lab has found that hyperthermia can efficiently potentiate the cytotoxic effects of the metallated enediyne. Here we describe the effects of one novel metalloenediyne, (Z)-N,N1-bis[1-pyridyl-2-yl-meth-(E)-ylidene] octa-4-en-2,6-diyne-1,8-diamine (PyED), on pancreatic cancer cells (Paca 2) and breast cancer cells (MDA 231) when treated with the compound at 37°C or 42.5°C. It was found that heat potentiated the effects of the drug on both cell lines when it was administered for 1 h. The drug was also tested on normal pancreatic cells (H6C7). Decreased growth was observed at relevant concentrations. Thus, it may not be practical to pursue this compound for treatment of pancreatic cancer. However, significant potentiation by heat was present with the breast cancer cells with little to no effect on the normal breast cells (HMEC) at 37°C. These data accumulated lead to the possibility of systemic administration of the drug for breast cancer. The evidence also suggests that hyperthermia treatment locally at a tumor in combination with the modified enediyne is a possible modality for clinical relevance.
Elevated Levels of Platelets and MDM2 Expression are Contributing Factors to Facilitating the Metastasis of Osteosarcoma

Osteosarcoma (OS) is the most common form of primary bone cancer and the 6th leading cause of cancer in pediatric patients. A chart review of OS patients treated at this institution suggests that high platelet counts at diagnosis is significantly (p=0.023) and inversely associated with first year survival. Extensively researched effects of platelet interaction with OS suggest that platelets facilitate tumor metastasis. Also, the most important prognostic factor for OS patient survival is metastasis to the lungs. Thus, we hypothesized that platelets increase metastasis to the lungs and reduce survival. Therefore, we tested whether increasing platelet numbers in a well characterized OS mouse model would decrease survival and/or increase metastasis to the lungs. We found that thrombopoietin (TPO) treated mice had increased platelet numbers, died earlier than placebo treated controls, and that lungs from TPO treated mice contained a small number of large tumor cells, whereas placebo treated lungs showed no signs of metastases. Next, a tissue microarray (TMA) was built from OS patients seen at our institution over the past 10 years. Mdm2, p53, TPO, and c-mpl expression were evaluated by immunohistochemical (IHC) staining followed by quantitation using the Aperio Imaging software. C-mpl (TPO receptor) expression was higher in the metastatic than the primary tumors, suggesting platelets contribute to the metastasis of OS. Elevated levels of Mdm2 correlated with metastasis and lower levels of p53, detected by IHC. In conclusion, the mouse model and the human OS data were similar, suggesting platelets and Mdm2 promote metastases in OS.

Mindfulness Effects on Depression and Anxiety Post-Stroke

Purpose: Depression and anxiety seem to be closely associated with stroke and can negatively affect stroke recovery and quality of life. Mindfulness Based Therapy (MBT) has been used as a treatment to reduce the symptoms of depression and anxiety, but there has been little known about the relationship between mindfulness, depression, and anxiety. This research project explored the relationship between mindfulness, depression, and anxiety.

Method: 12 post-stroke veterans from a yoga study (study A) and 11 post-stoke veterans who participated in a Group Occupational Therapy Fall Prevention after Stroke (GOT falls?) program (study B) were given the Freiburg Mindfulness Inventory (FMI), 9-item Patient Health Questionnaire (PHQ-9), and the Generalized Anxiety Disorder 7-item Scale (GAD-7) to measure mindfulness, depression, and anxiety.

Results: Overall, the post-stroke veterans tended to score high on the FMI and low on the GAD-7 and the PHQ-9. There was a strong and significant relationship between the GAD-7 and FMI (r=-0.826) (p=0.002) in study B.

Conclusion: The post-stroke veterans in these studies scored high on mindfulness and low on anxiety and depression. It appears from this small sample that there could be an inverse relationship between mindfulness, anxiety, and perhaps depression. Consequently, MBT may have a positive impact on individuals with anxiety and depression.
TRPC expression regulation in pig coronary artery smooth muscle cells

Atherosclerosis is a risk factor for myocardial infarction, which is one of the leading causes of death worldwide. Atherosclerotic coronary arteries are prone to vasospasm; in up to 60% of cases, coronary vasospasm occurs at a pre-existing atherosclerotic site. It has been reported that coronary artery vasospasm worsens the outcomes of patients with myocardial infarction. However, the mechanisms underlying increased spasticity of atherosclerotic coronary arteries are poorly understood. Histamine is a powerful vasoconstrictor in pig coronary arteries. Therefore, we used the hormone to compare the receptor-induced Ca2+ increases and contractions in control versus atherosclerotic pig coronary artery rings. We found that atherosclerotic coronary arteries exhibit increased spasticity compared to lean, control coronary arteries. Our data indicate that this results at least in part from increased Ca2+ influx through non-selective TRPC channels. We identified a component of atherosclerotic pig blood plasma that regulates TRPC expression in pig coronary arteries. The understanding of the molecular mechanism resulting in upregulation of TRPC expression will help to develop methods to better control vasospasm in atherosclerotic patients.
Chart Review of Presenting Psychopathology in Drug-Exposed Children

In utero exposure to drugs of abuse impacts cognitive, motor and emotional development from the neonatal period through adulthood. While the impact of drugs of abuse on cognition has been well documented, the nature of emotional impairments, as manifested by childhood psychiatric disorders, is less clear. The present study focused on characterizing the psychopathology of in utero drug-exposed children seeking outpatient psychiatric care. We hypothesize that children with in utero drug exposure will present with high rates of disruptive behavior problems. Thirty children (23 males, 7 females) were selected, based on caregiver-report of in utero exposure to one or more of the following: opiates, benzodiazepines, tobacco, alcohol, marijuana, or stimulants in utero. The average age of the participants was 7.4 years old. 83.3% self-reported as Caucasian, 6.7% African American, and 10% Bi-racial. Of these 30 children, 66.7% came from families with low socioeconomic status, 13.3% lower-middle, and 20% middle. 17.4% had been exposed to opiates, 12.5% to benzodiazepines, 52% to tobacco, 60.7% to alcohol, 36% to marijuana, and 82.6% to stimulants. 13.3% was referred by child services, 20% by a pediatrician or neurologist and the rest were self-referred. The sample had an average of 2.13 DSM-IV defined psychiatric disorders. Chief complaints were: 40% behavior issues, 3.3% hyperactivity, 6.7% aggression, and 16.7% other (possible bipolar disorder, many different problems, self-injury and depression, or current medications were not effective).

Based on this chart review, most children were exposed to more than one substance while in-utero. As hypothesized, relative to other psychiatric disorders, these children have an increased risk for externalizing psychiatric disorders, although most met criteria for multiple disorders, across classes. Additional research is warranted on specific psychiatric treatment needs of in utero drug exposed children, as they present at high rates for psychiatric treatment with a wide range of severe psychopathology.

Astrocyte reactivation in the hippocampus following traumatic brain injury

Traumatic brain injury (TBI) is an important medical concern because it can lead to long-term cognitive and emotional difficulties and behavioral disturbances. There are no effective treatments for these disorders. It is estimated that more than 320,000 U.S. veterans of the wars in Iraq and Afghanistan have sustained traumatic brain injuries (mTBIs) from blast waves of war-time improvised explosive devices, and 1.5 million civilian incidences of TBIs annually in the United States. Astrocytes are non-neuronal cells of the central nervous system. They play critical roles in supporting and modulating neuronal functions in the physiological conditions. It has been shown that TBI activates astrocytes, which play both harmful and beneficial effects to brain. It will be important if it is possible to modulate astrocyte response in the purpose of promoting their beneficial effects and reducing the harmful effects. However the molecular and cellular mechanisms controlling the astrocytes activation are still poorly understood. Here, we assessed the astrocyte activation at different times after TBI using immunostaining with antibody against glial fibrillary acidic protein (GFAP), an astrocyte’s specific marker. We found that astrocytes rapidly respond to TBI by exhibiting hypertrophy within 48 hours after injury. The reactive astrocytes then re-entered the cell cycle to proliferate from 72 hours after injury. The total number of astrocytes subsequently increased dramatically. Further studies showed that the mammalian target of rapamycin (mTOR) signaling, a critical signaling involved in the mediation of cell survival and proliferation, was activated in the reactive astrocyte. Inhibiting mTOR signaling reduced astrocytes reaction to TBI, indicating mTOR signaling is required for astrocyte reactivation. These results indicate that the astrocytes become exceedingly responsive through activating mTOR signaling as more time passes following TBI infliction.
Traumatic Brain Injury Leads to Aberrant Migration of Adult-Born Neurons in the Hippocampus

Traumatic brain injury (TBI) is the leading cause of death in children and young adults, leading to substantial cognitive impairment, motor dysfunction and epilepsy. There is no effective treatment for these disorders. The discovery of neural stem/progenitor cells (NSCs) in the adult brain raises a potentially promising strategy for repairing CNS injury. Our previous study showed that TBI promotes NSC proliferation in an attempt to initiate innate repair and/or plasticity mechanisms. However, the spontaneously post-traumatic recovery of hippocampal-related cognitive and memory functions is very limited. Better understanding of neurogenesis following TBI may provide additional intervention to further enhance neurogenesis for successfully repairing the damaged brain following TBI. Although newborn neurons generated from NSCs are continuously added to the brain throughout our life, they must migrate from their birthplace to their appropriate destination to develop into mature neurons. When we tracked the migration of newly generated neurons in the adult hippocampus after TBI, we found that a large percentage of immature neurons migrate pass their normal stopping site at the inner granular cell layer, and misplace in the outer granular cell layer of the hippocampal dentate gyrus. The aberrant migration of adult-born neurons in the hippocampus occurs 3 days after TBI, and lasts for 10 weeks, resulting in a great number of newly generated neurons misplaced in the outer granular layer in the hippocampus. The newborn neurons at the displaced position will not be able to make correct connections with their appropriate targets, and may even make wrong connections with inappropriate nearby targets in the pre-existing neural network. Abnormal migration has been shown to cause several diseases including dyslexia, schizophrenia, and epilepsy. These results suggest that stimulation of endogenous adult neural stem cells following TBI might offer new avenues for cell-based therapy. Additional intervention is required to further enhance successful neurogenesis for repairing the damaged brain.

Inter Eye Concordance in patients with Primary Open Angle Glaucoma (POAG)

Purpose: Glaucoma is one of the leading causes of blindness worldwide. The most prevalent form is primary open-angle glaucoma (POAG). Glaucoma progresses slowly and results in the loss of vision that begins in the periphery. 7% to 25% of the people who have POAG in one eye will develop it in the fellow eye over the period of 8 years. The purpose of this study is to determine if the visual loss appears in the same area of the visual field in the fellow eye and whether it follows the same spatial pattern over time as in the initially affected eye.

Methods: Ten patients with POAG were included in this retrospective study. All patients had clinical evidence of POAG in at least one eye, open angles, a best-corrected visual acuity of 20/50 or better, spherical and cylinder refraction within ±5.0 and ±3.0 diopters respectively, and at least six consecutive and reliable Standard Automated Perimetry (SAP) 24-2 tests in each eye (taken at least six months apart from each other). The concordance ratio between abnormal visual field locations between the two eyes was calculated.

Results: The proposal for the study was accepted by the Institutional Review Board. Patients meeting the inclusion criteria were successfully identified. Results are expected to show concordance between abnormal locations between the two eyes, which can be further extended and tested on larger datasets.

Conclusion: This work has clinical relevance in that it can lead to early detection and treatment in the fellow eye, thus preserving vision.
**Effects of Interstitial T Cell Activation Following Recovery from Ischemic Acute Renal Failure**

Salt sensitive hypertension and chronic kidney disease following recovery from acute kidney injury may occur secondary to incomplete repair or by activation of circulating factors stimulated by injury. We created a pilot study analyzing the effects of infiltrating interstitial lymphocytes in renal injury Sprague Dawley rats isolating the effects of direct versus remote injury via unilateral (UNX) nephrectomy after 5 weeks. These specimens were then stressed with a high salt diet (0.4% to 4.0%) for 4 weeks. We found a significant amount of activated CD4+ T Helper cells present in the direct injury model at day 34. These numbers were exacerbated when compared to the direct injury model that had the remote kidney excised and stressed by a high salt diet until day 54. Athymic nude rats were used in a secondary study to determine if T cells influence chronic kidney disease as these animals should not produce T cells. A heterozygous donor group was injured to induce T cell proliferation in their kidneys. At day 35, these T-cells were removed, cultured and injected into a portion of the initial study population via adoptive transfer. There was a noticeable reduction in creatinine clearance and an increase in albuminuria in the adoptive transfer specimen that is less noticeable in the regular athymic rats. With the data present from this pilot study, it can be reasoned that interstitial t-lymphocytes exacerbate issues associated with salt sensitive hypertension and CKD secondary to the AKI.

**Betaine transport in mouse hepatocytes and effect of hypertonic stress**

Betaine is an osmolyte and methyl donor in the kidney and liver, respectively. In the kidney medulla, it is used to balance extracellular hypertonic stress. It enters medullary cells via a sodium-dependent transport protein, known as the betaine/GABA transport system (BGT1), which is upregulated in response to hypertonic stress (Kempson, 1998). It was recently shown that BGT1 is more abundant in the liver but its function is unknown (Zhou, et al., 2012). In the present study, hepatocytes were used to investigate betaine transport. These cells were obtained from anesthetized mice by collagenase perfusion of the liver. Isolated cells were plated for 1-4 days in Williams E medium. Betaine uptake in hepatocytes was measured for various time intervals in buffered isotonic solution containing 0.1 mM [14C]betaine and in the presence and absence of 100 mM Na+. Intracellular [14C]betaine was measured by scintillation counting. Betaine uptake was increased in the presence of extracellular Na+ compared to replacement of Na+ with N-methyl-D-glucamine, proving that the uptake of betaine into liver hepatocytes is a Na+-dependent process. Healthy hepatocytes plated for 24 hours showed BGT1 protein present in the plasma membrane, as detected by immunohistochemical staining. Cells plated for 4 days showed a drastic change in appearance suggesting the hepatocytes changed morphology to adapt to a new environment. Overnight incubation of hepatocytes in hypertonic growth medium (400 mOsm) upregulated Na+-dependent betaine transport, suggesting a normal response to hypertonic stress. Further studies are needed determine if BGT1 is the primary pathway of betaine uptake by hepatocytes.