Program Description:
The Bridges to the Baccalaureate program is collaboration between IUPUI and Ivy Tech Community College of Central Indiana. Its goal is to provide underrepresented minority Ivy Tech students with the resources to successfully complete an associate’s degree and seamlessly transfer to a bachelor’s degree program in a biomedical or life science area.

The Bridges Program provides students with resources such as financial support, faculty mentoring and advising, and participation in a faculty-mentored research project at IUPUI.

The Bridges Program is funded by the National Institutes of Health.

Program Leadership:
Andy Gavrin, Ph.D., Principal Investor
Vicki Bonds, MS, M.Ed., Program Manager
**HAND2 MUTATION DETECTION IN TRICUSPID ATRESIA PATIENTS**

**Elijah H. Barry** (Anthony B. Firulli), Principle Investigator at IUPUI Dept. Pediatric Research

Tricuspid Atresia (TA) is a congenital heart disease in which the tricuspid valve is missing or abnormally developed. The defect blocks blood in the right atrium from flowing directly into the right ventricle. It is an uncommon form of congenital heart disease that affects about 5 in every 100,000 live births. While the cause of TA is unknown, Firulli lab data shows that in mice loss of transcription factor Hand2 function within a population of cells that line the inside of the heart (the endocardium) results in a TA phenotype. Hand2 is a protein that belongs to the basic helix-loop-helix family of transcription factors, and has been shown to play many different roles in embryonic development. To test whether loss of Hand2 function in human's results in TA, we began sequencing the HAND2 gene in 25 TA patients. Polymerase Chain Reaction (PCR) was used to amplify the TA patient Hand2 alleles. We then performed a TOPO ligation to insert the amplicons into a plasmid, followed by a transformation and minipreps to isolate individual clones. The clones were then sequenced and then compared to known HAND2 sequences using a commercial sequencing service. In this manner the Hand2 DNA sequence for several patients was obtained and analyzed for mutations. This project will shed light on the cause of TA, and is currently still in progress in Dr. Firulli's Lab.

Funding provided by the National Institute of Health (NIH), Bridges to Baccalaureate Program (Bridges).

**THE EFFECTS OF EXERCISE ON BONE HEALTH IN A RAT MODEL OF TYPE 2 DIABETES MELLITUS**

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Type 2 Diabetes mellitus (T2DM) a serious international public health problem with devastating health consequences. This disease can negatively impact several body systems, including the skeleton. Individuals with T2DM can present with lower bone mass, which places them at a higher risk for fracture. The purpose of our research is to evaluate the individual and combined effects of endurance exercise and impact loading on bone structure and strength in rats with diet induced T2DM. A rat model was used in our experiment because they are genetically similar to the human genome. Thirty-six diabetic Sprague-Dawley (ZDSD) rats were randomized to one of three groups: 1) cage controls (n=12); 2) treadmill running (n=12); and 3) jumping (n=12). Rats allocated to the treadmill running group ran for 30 minutes per day, 5 days/week at a 0% incline, while rats in the jumping group performed 50 drop jumps per day at a height of 35 cm, 5 day/wk. All rats were fed a high-fat diet to induce diabetes. All animals exercised for a total of 8 weeks, after which the femur, tibia, and spine were removed for analysis. Analyses included imaging (to evaluate bone structure), mechanical testing (to evaluate bone strength) and histological measurements to determine changes in bone formation. To calculate histological indices of bone formation all rats were given injected with the fluorochrome labels calcein and alizarin 10 and 4 days prior to sacrifice. It is anticipated that jumping and running will prevent the deleterious impact of Diabetes on bone architecture and strength and will enhance the amount of bone formed. The results from this study have important implications for improving bone health in individuals diagnosed with T2DM with non-pharmacological intervention strategies. Rats were also used in the experiment because they are closely related to humans when it comes to the body’s consumption of Glucose (sugar).
In recent years, cancer has ruthlessly taken many lives. Many forms of cancer have proven to be incurable, so a good sense of well-being and significant meaning of life is important before death. Although there have been a few programs that have focused on death-related concerns of dying patients, none have included the partner. Relationship issues have surfaced as one of the crucial concerns for patients, especially at the end of life. The stress of a patient also affects the partner’s well-being in the long run. The intention of this intervention is to lessen death-related stress for cancer patients and their partners. Cancer patients and their partners will be selected through a screening process through the IUSCC cancer center for a four-week intervention. The patients and partners then will take a pre-intervention assessment (Quantitative) followed by the intervention (Qualitative) itself. After the intervention, the patients and partners will take a post-intervention assessment (Quantitative). When analyzing, we will be looking for themes in the data and we will see if the numbers have improved from the pre-assessment to the post-assessment. The findings from the qualitative and quantitative data will be used to assist in the improvement of cancer interventions and the updating of current practices which will enhance its efficacy.

Funding provided by the National Institute of Health (NIH), Bridges to Baccalaureate Program (Bridges) and RESPECT Signature Center at Indiana University–Purdue University Indianapolis.
UNOBTRUSIVE TECHNOLOGY IN HEALTHCARE WORKFLOWS

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This research explores the implementation of technology that has a minimal or no impact on current workflow and as thus makes adoption less stressful. Many people fear technology, and think that it will make things more complicated and demanding. Understanding workflow and integrating technology in the workflow is crucial for its successful adoption. This research will evaluate the e- pen technology for its (1) efficiency and accuracy in capturing written text and (2) its fit into the current workflow of health care professionals. The adoption of technology in healthcare has improved in the last couple years mainly due to the ARRA incentive program (Bowens, Frye, & Jones, 2010), but it is still slow in reference to the business world (Why Health IT," 2011) The main issue for slow adoption of technology in health care remains the lack of integration technology in a meaningful way into the existing clinical workflow despite the fact that studies show that implementation of HIT may improve health outcomes, reduce medication errors, augment chronic disease management, reduce health disparities, and offer substantial cost savings. (Ammenwerth, Gräber, Herrmann, Bürkle, & König, 2003). The study proposes to use the following steps to evaluate the feasibility of the e-pen (e.g., Smart pen) in clinical practice: test of the smart pen (benefits, barriers); test of accuracy of pen (non-clinical setting); and usability test in clinical setting (replication of Clinical Assessment Forms).

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ASSESSMENT OF PROCEDURAL ASPECTS AND QUALITY CONTROL IN HUMAN PLACENTAL RNA ISOLATION PROTOCOLS

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High quality RNA is of paramount importance in accurately interpreting gene expression changes in the placenta throughout pregnancy, as well as in common placental pathologies. The purpose of this study was to develop a standard operating protocol for the collection of human placental tissue and isolation of high quality RNA for pregnancy-related molecular studies. To accomplish this task, we compared several different parameters to minimize RNA degradation, including preservation (liquid nitrogen vs. RNAlater), disruption (mortar/pestle vs. homogenization), and isolation (Trizol vs. RNeasy). We performed 150 RNA isolations from 30 term placentas. The A260/280 ratio for all samples was 2.11 ± 0.1 (mean ± s.d) and the RNA quality indicator (RQI) was 7.1 ± 1.4 (mean ± s.d). No significant differences in RNA purity, or quality were observed between different placental collection and RNA isolation techniques. However, poor RQI values of 2.7 to 3.3 were obtained after brief thawing of frozen placental samples. In addition, we compared storage of RNAlater stabilized tissue at 4°C or room temperature for 1, 7, or 30 days. The RNA integrity of specimens stored at room temperature for 30 days was significantly lower (p<0.05; RQI 5.0 ±1.2, mean ± s.d) than specimens stored at room temperature for 1 day (RQI 7.3 ± 0.58). We also tested pooled placental RNA that was isolated using either the TRIzol or RNeasy kits for the presence of inhibitory factors using a qPCR assay. Our results showed the absence of inhibitory factors in all samples (Cp 22.49 ± 0.16, mean ± s.d) compared to the negative control template (22.80 ± 0.18, mean ± s.d). The results of these studies will be useful for establishing standard procedures for placenta tissue collection for pregnancy biobanks.

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Exploring Factors Related to Non-Medical Prescription Stimulant Use among College Students

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Studies have shown that more individuals are abusing prescription drugs than drugs such as cocaine, heroin, and ecstasy. The purpose of this study is to better understand this abuse among U.S. college students and to identify current prevalence rates, risk and protective factors, effective interventions, and future recommendations. It is anticipated that results will show that stimulants are the most commonly abused prescriptions among this population. Although reasons behind the abuse vary, most reported usage to prevent a loss of concentration and to help them study. Others reported doing so primarily to experiment or to get high. However, in almost all cases, individuals inclined to abuse prescription drugs were also more likely to engage in other substance abuse. Thus, prescription drug abuse in college may be an early indicator of future substance abuse concerns.

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THE EFFECTS OF HYPOXIA-INDUCED PULMONARY HYPERTENSION ON MEDIATORS OF CELLULAR PROLIFERATION IN THE LUNGS AND RIGHT VENTRICLES OF RATS

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Pulmonary hypertension (PH) occurs when the small arteries of the lungs become narrowed and occluded. This makes it difficult for blood to pass through and pressure begins to build up. Overtime when this continues to occur, due to chronic pressure overload the right side of the heart becomes enlarged. PH can be influenced or caused by numerous factors such as blood clots in the lungs, congestive heart failure, low oxygen levels, lung disease, etc. Symptoms that patients with pulmonary hypertension may encounter include: chest pains, fatigue, dizziness, leg and ankle swelling, bluish skin color, and weakness. Doctors may perform diagnostic tests like blood tests, cardiac catheterization, chest x-ray, echocardiogram, and CT scan. In the research setting, rats are frequently used to study the disease. Dr. Lahm created a model similar to humans using two different groups of rats. One group of rats was kept in normoxic conditions (normal oxygen levels), and the other group of rats where put into a hypoxia chamber (low oxygen levels; 10% oxygen for two weeks). After the two weeks, the rats are euthanized and morphological changes as well as changes in proteins that regulate growth of cells in the heart and lungs are analyzed. We found that the hormone estrogen decreases the degree of pulmonary hypertension in rats. Male rats are therefore being injected with estrogen, and the lab is investigating if and how certain proteins that are altered by hypoxia are normalized by estrogen. There currently is no cure or treatment for PH. Even though some forms of PH are being treated with medications, these drugs don’t always work well, and our hope is that this research will lead to new therapies for this devastating disease.

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EVALUATION OF THE EFFECTS OF GREEN TEA EXTRACTS ON BONE HOMEOSTASIS IN THETs65DN DOWN SYNDROME MOUSE MODELS

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Down Syndrome (DS) is a genetic disorder resulting from trisomy of chromosome 21, which causes cognitive impairment, craniofacial abnormalities, low muscle tone, and skeletal deficiencies. To study these phenotypes, I utilized the Ts65Dn mouse model, which contains three copies of approximately half the orthologues found on chromosome 21 and exhibits cognitive, craniofacial and skeletal deficits similar to the phenotypes found in humans with DS. Individuals with DS and Ts65Dn mice have deficits in bone mineral density (BMD), architecture, and bone strength. Over-expression of Dyrk1a, a serine-threonine kinase encoded on chromosome 21, has been linked to deficiencies in DS bone homeostasis. Epigallocatechin-3-gallate (EGCG), an aromatic polyphenol found in high concentrations in green tea, is known to inhibit Dyrk1a activity. Normalization of Dyrk1a activity by EGCG may have the potential to regulate bone homeostasis and increase BMD and bone strength in individuals with DS. In this study, it hypothesized that EGCG obtained from different sources would have differential effects in correcting bone deficits associated with DS. To test our hypothesis, we performed High Performance Liquid Chromatography on EGCG and related compounds from different sources. Next, I treated three-week-old Ts65Dn and control male mice with EGCG for three weeks. Every two days, EGCG intake was measured and mice were weighed. At six weeks of age, mice were killed and, DXA and microCT analysis were used to assess trabecular and cortical BMC and BMD of femurs, skulls and mandibles of male mice. A three-point bending test was used to assess bone strength, point of failure, and fracture risk of femurs. The results will provide an important comparison between pure EGCG and

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Poster # 7

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Poster # 13
those that were purchased from other vendors on correcting skeletal deficits associated with DS.

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CYP2C19*17 GENOTYPING IN PREGNANT WOMEN WHO TAKE PROTON PUMP INHIBITORS

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Cytochrome P450 is a group of proteins within liver cells (hepatocytes) that are and are necessary for the metabolism of the majority of drugs. One specific sub-family of Cytochrome P450 is CYP2C19. This protein is known to specifically metabolize a family of drugs known as Proton Pump Inhibitors (PPI). PPIs function by blocking enzymes that produce stomach acid. This class of drug is used with individuals who have Gastroesophageal Reflux Disease (GERD). It is known that 30-80% of pregnant women experience GERD throughout their pregnancy [1]. This study focuses on the CYP2C19*17 genotype of women who were taking the PPIs, omeprazole, esomeprazole, and pantoprazole during their pregnancy. Alleles of CYP2C19*17 are predicted to indicate differing rates of metabolism of PPIs. In a clinical study done by the department of genetics and genomic sciences, alleles T/T and C/T are predicted to have ultra-rapid metabolizing functions, while C/C is predicted to be an extensive metabolizer [2]. Our study included 27 women who were taking PPIs during their pregnancy. We found that only 28% of our sample population genotyped for ultra-rapid metabolism (T/T or C/T) and 72% genotyped for intermediate metabolism (C/C). This research suggests that genotypes may be used to design individual treatment regimens for patients in order to maximize efficiency of omeprazole, esomeprazole, and pantoprazole.

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Alcohol Alters the Spatial and Temporal Expression of DNA and Histone Methylation in Mouse Embryos

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Alcohol has been observed to have teratogenic effects during different stages of embryonic development. These effects can be condensed under fetal alcohol spectrum disorder (FASD), exhibiting a variety of signs from growth retardations to neurobehavioral aberrations. Despite better understanding of several potential mechanisms, the question of how alcohol, as an environmental factor leads to brain growth delay in FASD remains elusive. DNA methylation is key to development and tissue specification. Studies have suggested that alcohol may alter gene expression by affecting DNA and histone methylation. Previous studies have demonstrated that 5-methylcytosine (5mC), a DNA methylation mark, is associated with histone 3 lysine-9me3, (H3K9me3) to play a role in gene repression. Recently another methylation mark, 5-hydroxymethylcytosine (5hmC), was found to prevail in the nervous system. However, its function has not been clear. Global analysis suggests that it is a transition of demethylation leading to transcription. This study aims to identify the association of 5hmC with histone 3 lysine-4me3, (H3K4me3) a transcriptional activator in gene
expression, and then study 5hmC under influence of alcohol exposure. This study will utilize both an in vivo model—the vapor chamber, and an in vitro model—the embryonic culture system to address this question. The study will then compare the DNA methylation marks, and histone modification marks to see if the spatial and/or temporal distribution has been affected by alcohol exposure. Embryos were exposed to alcohol (400mg/dL, 88mM) from the beginning of embryonic day (E) 8 for 6hrs, harvested at E10, and processed for immunohistochemistry. It is expected in the alcohol-treated embryos that an overall retardation of embryonic growth, delayed neural tube formation, and altered expression of epigenetic markers will be observed. This study could indicate that alcohol, through alteration of DNA and histone methylation is a potential mechanism underpinning brain growth delay in FASD.

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