ABSTRACTS IN DEVELOPMENT: RESULTS PENDING

Research from The National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, and Charles R. Drew University of Medicine and Science 2007 High School Student Summer Research Program

DEVELOPMENT IMPACT INJURY RISK

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Mentor: Gayane Stepanian, MA, University of Miami, School of Medicine, Miami, Florida

Injuries are damage done to the body in the form of electrical, chemical, or thermal energy or from the absence of heat or oxygen. Accidents are random occurrences that can be prevented. Many children are affected by being injured. The first three years of a child's life build the foundation for healthy growth and development. The brain is activity-dependent, so it grows from experience. This period can be seriously hindered and have long-term and lifelong implications if a serious injury occurs. Research has shown that injury is the leading cause of death for children 0–18 years of age, but the group of 0–3 years of age have the highest prevalence of injury. But why this age group? We hypothesized that this age group is at the highest risk for injury because they are new to the world, inexperienced, and underdeveloped.

In order to test this hypothesis the author served as an intern at the Injury Free Coalition for Kids of Miami. The internship offered an opportunity to review child injury literature, experience research-based practice with child safety educators and explore if, why and how children are at the highest rank for injury death and injury related hospitalization during 0–3 years of age.

SITE DIRECTED MUTAGENESIS: YEAST VMA4 SUBUNIT E

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V-ATPases are groups of enzymes that act as proton pumps to acidify certain parts of the cell to keep a homeostatic pH. The two different domains of the enzyme have been identified as V_1 (the region above the cytoplasm) and V_0 (the region within the cytoplasm). The V_1 domain is responsible for the hydrolysis of ATP into ADP and a free phosphate ion. V_0 is responsible for pumping and rotating protons around the cell to keep a viable pH for the cell to survive.

It has been hypothesized that a component of this enzyme within the V_1 domain labeled subunit E is used for support of the V_1 domain in yeast cells. Therefore, without subunit E the enzyme would break apart and cease to function. To test the hypothesis, a site-directed mutagenesis will be performed on the VMA4 gene of a yeast cell to mimic the gene in humans. In yeast the V_1 domain of the V-ATPase disassembles when there is a lack of glucose, but when glucose returns to the cell, the enzyme reassembles in a process known as reversible disassembly. Humans have the same enzyme within their sperm and kidneys and it does not disassemble. So if the E subunit is directly responsible for support, then the mutation that we perform on it should make it unable to disassemble.

COMPARISON OF URINE, MECONIUM, AND VERNIX SPECIMENS FOR TOXICOLOGY SCREENING IN NEWBORN INFANTS

Student Researcher: Kamila Lambert, Menlo High School
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Nationally, 7.7% of women are reported to have abused illicit drugs during pregnancy. Perinatal substance abuse can result in both prematurity and low birth weight in infants that may have subsequent health complications after birth. The Labor and Delivery Department at San Francisco General Hospital delivers approximately 20 neonates per month whom physicians suspect may have been exposed to drugs of abuse in utero. Standard screening techniques for documenting gestational drug exposure utilize urine and more recently meconium. Urine specimens, however, can be difficult and time-consuming to collect, and may only detect recently used illicit drugs. Meconium has been utilized as a specimen for drug toxicology screening to detect a longer period of gestational substance exposure and is easy to collect, but is a difficult material for analysis as the extraction is labor intensive and therefore costly. Vernix is easily collected at birth in many newborns and could be a specimen able to detect long-term drug exposure during gestation. Our clinical laboratory previously developed methods for vernix screening for illicit drugs (opiates, cocaine, and amphetamines). This study was undertaken to compare vernix and meconium samples to standard, clinically indicated urine toxicology screens for illicit drugs in an inner-city teaching hospital.

THE EFFECT OF COQ10 ON THE BCL-2 FAMILY IN MELANOMA EXPRESSION OF BIM IN SKMEL-28 CELLS WITH COQ10 TREATMENT AT TIME DEPENDENT INTERVALS

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Mentors: Indushekhar Persaud; Niven R. Narain, Department of Dermatology, Leonard M. Miller School of Medicine University of Miami, Florida

The role of the particular pro-apoptotic BH3-only protein Bim is the focus of our study. Bim is found in the mitochondria and has three known isoforms that are obtained by alternative splicing that result ± in Bim_{EL} 23 kDa, Bim_L 15 kDa and Bim_S 12 kDa. The role of Bim has been noted to induce apoptosis by somehow interacting with Bax/ Bak to stimulate cytochrome c, or by inhibiting and or antagonizing anti-apoptotic proteins such as Blc-2.

Skmel-28, a melanoma cell line, was cultured and treated with varying concentrations of coenzyme Q10 (CoQ10). Coenzyme Q10 can be found in every cell of the body, in both the plasma membrane and the mitochondria. It aids in the diffusion of electron between complexes in the electron transport chain. Several studies are currently in process analyzing the effect of antioxidants such as CoQ10 with cancer therapies.

ANALYSIS OF TRANSBILAYER FLIP FLOP OF PHOSPHOLIPIDS BY ENDOPLASMIC RETICULUM PROTEINS

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Biogenic membranes are made of phospholipid bilayers. Phospholipids are made up of two hydrophobic tails and a hydrophilic (polar) head group. Phospholipids are synthesized on the cytoplasmic face of the endoplasmic reticulum (ER) membrane. In order to create a uniform bilayer, phospholipids must be transported from the cytoplasmic face to the outer face of the membrane. The hydrophilic head group cannot pass through the hydrophobic region of the membrane thus a transporter is needed. In a model system lacking ER proteins it takes hours for phospholipids to flip across the membrane.If, however, we add ER proteins to the same system, phospholipid movement across the membrane (flipping) occurs with a half time of ~3 minutes. Thus there is presumed to be a specific protein(s) termed flippase(s), which are involved in the flipping of phospholipids. These proteins are not yet identified but their activity can be measured in vesicles made with a mixture of ER proteins and phospholipids containing fluorescent head group nitro-benxadiazole-phosphatidylcholine (NBD-PC). NBD-PC is a marker to track movement of phospholipids across the membrane. The nitro group on NBD-PC is a fluorophore. Fluorophores have the ability to absorb specific wavelengths of light and emit energy at a lower wavelength. In the reconstituted vesicles we ideally expect there to be a ~50% distribution of NBD-PC phospholipids across the membrane. Total fluorescence is measured using a fluoremeter, which emits an emission wavelength that excites the nitro group causing it to emit energy in the form of light that is recorded by the fluorometer. After the total fluorescence is measured dithionite is added. Dithionite is a quenching substance that reduces the nitro group on NBD-PC to an amino group causing it to lose its ability to fluoresce. Dithionite can only reach NBD-PC on the outer membrane. Vesicles without flippase proteins will maintain the ~50% distribution of phospholipids from reconstitution so only ~50% of the NBD-PC will be quenched, causing a ~50% change in total fluorescence. As the amount of flippase proteins in the vesicles increase, the percent change in total fluorescence will also increase because more NBD-PC phospholipids will be flipped from the cytoplasmic face to the outer face of membrane where they can be quenched by dithionite. Using this assay we plan to take vesicles containing fluorescent phospholipids with a normal head group and larger head group and test the flippase activity. We predict that the normal head group will have more flippase activity than in the vesicles containing the larger head group. By determining the size of the phospholipid head group most functional with flippase, the size of flippase can then be deduced.

PYY AND GLP-1 EXPRESSIONS IN OBESITY PRONE AND OBESITY RESISTANT RATS

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Individuals are considered obese when their BMI>30. Previous studies have linked people becoming prone to obesity due to genetics/heredity, social status, and daily eating habits.

In our research we studied two groups of rats, the Osborne-Mendel rats, and the S5B/Pl rats. The Osborne-Mendel rats, who become obese when put on a high-fat diet, were split into two groups; the first group was put on a high-fat diet and the second group on a low-fat diet. The S5B/Pl rats, who do not readily become obese when eating a high-fat diet, were also split into two groups; the first group was put on a high-fat diet and the second group on a low-fat diet. Our goal was to find out the differences in the hormones located in the gut (distal intestine) of the two different groups of animals. These hormones send signals to the brain of these animals telling them to refrain from eating. We used real-time polymerase chain reactions to measure gene expression levels in the gut.

GROWTH DYNAMICS OF MARINE PHYTOPLANKTON

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Mentors: Dr. Alexandra Worden; Rory Welsh, Rosenstiel School of Marine and Atmospheric Sciences; Ishmael Sharpe, University of Miami, Jackson Memorial Hospital, Miami, Florida

The greenhouse effect as well as global warming is becoming a major issue due to the excessive amounts of pollution as well as the depletion of the ozone layer which helps block harmful ultraviolet rays. We have found that there are ocean-living microorganisms, identified as micromonas algae, performing the same procedure (ie, decrease the amount of carbon dioxide) as those of plants when they go through photosynthesis. We investigated the effects that nitrogen has on micromonas algae and whether or not it can live without nitrogen. Cultures were grown for many generations in different media containing different vitamins needed to grow; a set with both NH4 and NO3, a set with only NH4, a set with only NO3, and a set with no nitrogen at all. These cultures were continuously transferred during their growth period so that they remained in their mid-exponential stage of growth, giving the best results possible being that it is at their most active stage. After ten generations grown in the normal state containing all nutrients and nitrogen, they were divided into four new groups with the different media formulas. The purpose of this experiment was to determine whether the different concentrations of nitrogen would cause an increase or decrease in number of these microorganisms during different seasons of the year.

EXAMINING PTSD AMONG SOUTHEAST ASIAN COMMUNITIES WITHIN A CULTURAL FRAMEWORK

Student Researcher: Vi Le, Oakland Technical High School
Mentors: Erica Torres, PsyD; Nancy Quiggle, PhD, University of California, San Francisco, California

Southeast Asian refugees to the United States have suffered severe traumas, and face challenges in adapting to a new and unfamiliar land. In our study, we examined post-traumatic stress disorder (PTSD) across various Southeast Asian groups, including Hmong, Cambodian, Lao, and Vietnamese refugees. We began by providing a background of these groups and the traumas that they have experienced. We then reported prevalence rates of PTSD among various refugee groups. Finally, we discussed differences in utilization of mental health services, and how cultural factors influence these differences in the mental health field.

OPTICAL IMAGING OF TUMOR TARGETED NATURAL KILLER CELLS

Student Researcher: Julia Arzeno, Montavista High School
Mentors: Sidhartha Tavri, MD, Sophie Boddington, Reinhard Meier, MD, Lydia Mandrussow, Tobias Henning, MD, Karen Hagberg, Heike Daldrup-Link, MD, PHD; Contrast Agent Research Group, Center for Functional and Molecular Imaging, Department of Radiology, University of California, San Francisco, California

New immunotherapies against cancer are based on natural killer (NK) cells, specialized white blood cells, which have been genetically modified to specifically recognize and lyse cancer cells *in vivo*. The advantage of NK-cell based therapies compared to chemotherapy or irradiation is their high, selective cytotoxicity against tumor cells without toxicity against non-malignant cells. The aim of our study was to develop a technique for non-invasive imaging of tumor-targeting NK cells in order to monitor the *in vivo* distribution, tumor accumulation and tumor cytotoxicity of these cells. To reach this aim, we sought to develop a technique for *ex vivo* labeling of tumor-targeting NK cells with the cell-specific fluorescent dye, DiD, for subsequent depiction of the cells with OI. We expect to accomplish the following: a) label NK cells with a fluorescent dye, b) detect the fluorescence of the labeled cells with OI, c) determine what may interfere with the detection of fluorescence.

THE CONNECTION BETWEEN DIABETES AND ORAL CARE

Student Researcher: Darcielle Allen, Detroit School of Arts
Mentor: Eric Ayers, MD, Wayne State University School of Medicine, Detroit, Michigan

The purpose of this research project was to improve the overall wellness of patients with diabetes whose uncontrolled glucose levels can affect other parts of the body. Most people know about the effects of diabetes on eye health and foot health; but, what do people really know about the connection of diabetes and oral health? Patients at our local clinic appeared to have little knowledge of the relationship between oral health and diabetes. We propose the development of an educational tool specifically geared toward diabetes and oral health to improve the overall wellness of patients with diabetes.

COMPARISON OF COGNITIVE FUNCTION, QUALITY OF LIFE, SEXUAL AND PSYCHOLOGICAL FUNCTION IN WOMEN WITH HYPOPITUITARISM: THE ROLE OF ANDROGENS

Student Reseracher: Kiara Banks, King/Drew Magnet High School of Medicine & Science
Mentors: Erik Zuckerbraun, Ted Friedman, Charles R. Drew University of Medicine & Science, Los Angeles, California

The primary purpose of this study is to determine the effects of physiologic testosterone replacement on subjective and objective measures of sexual function, cognitive function and quality of life in women with hypopituitarism. A secondary purpose is to determine the effects of physiologic testosterone replacement on physical function in women with hypopituitarism. The role of testosterone in cognitive and psychological function in women remains poorly understood. Women with hypopituitarism have severely diminished ovarian and adrenal androgen production and thus represent an excellent model to study the consequences of androgen deficiency. We hypothesized that women with hypopituitarism would exhibit altered psychological function and decreased quality of life as a result of androgen deficiency, as well as objective measures of sexual function possibly related to androgen deficiency.

TESTOSTERONE STIMULATION OF CARDIOMYOCYTES ENRICHED BY SELECTION OF MURINE EMBRYONIC STEM CELLS WITH AN α-MHC PROMOTER PLASMID

Student Researcher: Jonathan Black, King/Drew Magnet High School of Medicine and Science
Mentor: Wayne E. Taylor, PhD, Charles R. Drew University of Medicine and Science, Los Angeles, California

Embryonic stem cells (ES cells) have been shown to be useful in therapeutic medicine (eg, healing damaged heart tissue). Since ES cells are totipotent, they have the ability to differentiate into any type of cell in the body; this is especially necessary for the regenerating of tissue in our bodies that have a low renewal capacity. Murine ES cells can be propagated indefinitely fed on a feeder-layer of mitotically inactivated mouse embryotic fibroblast (MEF) cells and allowed to differentiate into embryoid bodies and then cardiac muscle cells, including beating cardiomyocytes. In our lab we previously showed that testosterone can further stimulate their growth into cardiomyocytes. However, when this was done previously in our lab the testosterone only increased the amount of cardiomyocytes by 50% in which the total number was less than 1% of the original cells. We hypothesize that the solution to resolving this problem is to grow new ES cell lines using LIF (leukemia inhibitory factor) to help maintain the cell lines as ES cells. Then we will select for differentiation of cells that are cardiomyocytes by using ES cells containing a beta-MHC promoter plasmid containing a cardio-specific promoter (beta-MHC) linked to a gene for Puromycin-EGFP. This Puromycin-EGFP marker will allow us to select cells with the antibiotic for puromycin resistant cells of cardiac lineage, which should then have a green fluorescence due to EGFP protein expression. This should increase the percentage of cardiomyocytes that are in the culture and will allow us to study the T effect on them more easily. This project will hopefully contribute toward development of ES cell-based therapy for cardio infarction or congestive heart disease.

THE LINK BETWEEN CARDIOVASCULAR DISEASE, KIDNEY DISEASE, AND ABANDONED URANIUM MINES ON THE NAVAJO RESERVATION

Student Researcher: Justin Devore, Gallup High School
Mentor: Johnnye Lewis, PhD, DABT, College of Pharmacy, Health Sciences Center, University of New Mexico, Albuquerque, New Mexico

Recently, scientists have found that there is a high prevalence of cardiovascular disease in subjects with chronic kidney disease (The American Heart Association: *Circulation*. 2007; 116:85–97). Chronic kidney disease promotes hypertension and dyslipidemia, which in turn can contribute to the progression of renal failure. In the Navajo Nation, there are many abandoned uranium mines in close proximity to residents who may be exposed to possible toxins daily. The heavy metal uranium, not the radioactive portion, is known to cause damage to the kidneys.

Uranium, a kidney toxicant, would be likely to affect kidney health more than cardiovascular health. Therefore, we hypothesized that people living in areas exposed to uranium mine waste or tailings would have a weaker association between kidney and heart disease than people in unexposed areas. This research project is in the beginning stages. I will collect data from 17 different chapters in the Navajo Nation; of the 17 chapters, some are exposed to the uranium mine waste while others are not exposed. My data will result from a survey including three measures of cardiovascular disease and three measures of kidney disease.

My work might show that the people living near mines are more at risk of getting both cardiovascular and kidney diseases. Understanding the relationship between uranium, cardiovascular disease, and kidney disease is important to protect the people living near mines. This information will give the people a better understanding of the risks and it will help them take better care of their health.

A POSSIBLE ROLE FOR FORSKOLIN AS A REGULATOR OF ADHERENT JUNCTIONS ASSEMBLY AND STABILITY

Student Researcher: Ashley Mariani, Colegio Ponceño
Mentor: Pedro Santiago, PhD, Ponce School of Medicine, Ponce, Puerto Rico

Forskolin, a drug that increases intracellular cAMP levels by inducing the activity of the enzyme adenylyl cyclase, is also well known as an inhibitor of cancer metastasis, a cellular process by which cancer cells are shed from the primary tumor site and acquire the capacity to invade and colonize distant tissues and form new tumors. In this study, we are examining Forskolin's anti-metastasis properties at the cellular and molecular level by analyzing its effect on the stability and integrity of adherent junctions, which are membrane-associated protein complexes involved in cell-to-cell adhesion and that are known to be disrupted during metastasis. Given that adherent junction disruption with concomitant loss of cell-to-cell adhesion plays an important role during metastasis by allowing cell shedding from the primary tumor, and given Forskolin's inhibitory effect on metastasis, we want to determine whether Forskolin can prevent metastasis, at least in part, by promoting the assembly and stability of adherent junctions and by strengthening cell-to-cell adhesion. To test our hypothesis we will use human colorectal adenocarcinoma cells to determine the effect of Forskolin on the expression levels of adherent junction proteins alpha-catenin and E-cadherin as well as on the assembly of stable adherent junctions. To achieve our aims, we will compare Forskolin-treated and control cells in terms of alpha-catenin and E-cadherin expression using immunoblot analysis. Assembly and integrity of adherent junctions will be assessed by immunocytochemical labeling of alpha-catenin and E-cadherin in intact cells using the technique of indirect immunofluorescence.

TESTOSTERONE STIMULATION OF INSULIN-INDUCED GLUCOSE UPTAKE, AKT SIGNALING AND GLUT4 MEMBRANE TRANSPORT OBSERVED IN 3T3-L1 MOUSE ADIPOCYTES

Student Researcher: Nze Chijioke, King/Drew Magnet High School of Medicine and Science
Mentors: Dr. Wayne E. Taylor; Rajan Singh, Charles Drew University of Medicine and Science, Los Angeles, California

There are 20.8 million children and adults in the US with diabetes. When a person has diabetes mellitus, the cells of the body are either unable to recognize insulin or the body does not produce it. In patients with diabetes with insulin resistance, the effects of testosterone (T) administration are poorly understood. In men, lower testosterone in serum is associated with type 2 diabetes mellitus, while T treatment stimulates increased insulin sensitivity and glucose uptake into cells while decreasing fat mass. The purpose of this study is to measure effects of T on gene expression profiles of several genes involved in the insulin-signaling pathway in a preadipocyte cell line 3T3-L1 during differentiation in adipogenic medium, and to determine testosterone's effect on glucose uptake in adipocytes. The information obtained from this study may provide the rationale for targeting key components responsible for insulin resistance in patients with type 2 diabetes. By finding out the mechanism involved in glucose intake, we can discover ways to better treat patients with diabetes and reduce the danger of this disease.

THE MOLECULAR EFFECT OF NUTRITIONAL SUPPLEMENTS (MENS) TRIAL ON EARLY STAGE PROSTATE CANCER

Student Researcher: Kirsten Perez, Castro Valley High School
Mentor: Nannette Perez, University of California, San Francisco, California

As prostate-specific antigen (PSA) screening has become more widespread, more men are being diagnosed with low-risk prostate cancer. There are controversies regarding the over treatment of localized, low-risk prostate cancer. Men with low-risk prostate cancer do not necessarily require treatment and are therefore deciding to take part in active surveillance. Studies have shown that nutritional factors, such as omega-3 and lycopene can have an effect on the progression of prostate cancer. We hypothesize that the lycopene supplementation will decrease the serum levels of insulin-like growth factor (IGF) and that omega-3 will show the down-regulation of Cox-2 gene in the patients taking the supplements. The University of California, San Francisco, Department of Urology under the direction of Department Chair, Peter Carroll, MD is conducting a clinical trial examining the molecular effects of lycopene and omega-3 on men with low-risk prostate cancer. The study, The Molecular Effects of Nutritional Supplements (MENS) is a randomized, placebo-controlled, double-blinded clinical trial. Here, patients satisfying eligibility requirements will complete a dietary questionnaire prior to randomization. Based on these self-reports, patients will be stratified into four groups (low omega-3/high lycopene; low omega-3/low lycopene; high omega-3 /high lycopene; high omega-3/low lycopene). Patients will then be block-randomized into three regimens (placebo, omega-3, or lycopene) within these strata. Trans-rectal ultrasound guided prostate biopsies will be conducted at the beginning of the study and after the three-month intervention. The study will close to accrual shortly and results will be published after the analysis is completed.

KIDNEY TRANSPLANTATION SURVIVAL BASED ON RACE

Student Researcher: Nkemjika E. Egwin
Mentor: Donald Gerber, MD

The purpose of this research was to find out which patients have a newly transplanted kidney survive in their body longest based on race and type of transplant. The four race groups studied in this research were: Whites, African Americans, Hispanics, and Asians. The three types of kidney transplants studied were from living donors, deceased donors, and extended criteria donor (ECD) deceased donors. There are many factors that affect how long a newly transplanted organ will survive in the patients' body. Kidney transplants are one of the most common types of transplants done in the United States. Race is one of the many factors that are taken into consideration when it comes to answering the question of how long the transplanted organ will last in the patient. Our hypothesis is that Whites have a better graft survival rate due to their living habits and lower rates of disease.

Through our research, We found data on three different types of graft survivals in four different race groups. The United Network for Organ Sharing (UNOS) website was used as a reference for this research since it has records of all the transplants done in the United States. My results show which race has the longest graft survival with each type of graft.