9TH ANNUAL KEYS RESEARCH SHOWCASE

Friday, July 17, 2015
9:00 a.m. - 12:00 p.m.
Dear Friends, Supporters, and Participants,

Thank you for attending the 9th Annual KEYS High School Research Internship showcase and closing ceremony.

This year, 48 interns from across Arizona have completed the program. During the seven-week internship, they participated in a wide variety of research projects ranging from understanding the natural world to clinical research and toxicology. They have learned from each other and from the wonderful researchers, staff and laboratory teams who mentor them throughout the program.

We are very proud of each of them for the accomplishments they have achieved. After completion of the program, many interns are inspired to continue their research in college and participate in local research projects. This program becomes a stepping-stone for both their personal and career growth.

Essential to the success of the KEYS program, are contributions of time, talent and mentorship from the research faculty and their students at the University of Arizona. Interns are welcomed into the labs, made part of the team, and provided the opportunity to experience research by way of critical thinking and hands-on experiments.

As Co-Directors of KEYS, we personally thank you for your part in KEYS. Without the support of the UA, Tucson, and Arizona Communities, as well as all the donors and parents, inspiring the minds of these students and providing them with the experience to be part of a research team would not be possible.

Please join us in celebrating the achievements of the 2015 class of KEYS High School Research Internship Interns!

Marti Lindsey, Ph.D.
KEYS Co-Director
SWEHSC

Heather Ingram
KEYS Co-Director
BIO5 Institute
POSTER SESSION
9:00 a.m. - 10:30 a.m.

University of Arizona
Leon Levy Cancer Center,
Peter Kiewit Auditorium, Room #2951

1515 N. Campbell Avenue
Tucson, AZ 85721

Light refreshments served

PROGRAM
10:45 a.m. - 12:00 p.m.

Banner-University of Arizona Medical Center
Duval Auditorium, Room #2600

1501 N. Campbell Avenue
Tucson, AZ 85724

Welcome
Dr. Andrew Comrie,
Senior Vice President for Academic Affairs and Provost

KEYS Alumni Presentations
Mely Bohlman, 2014 KEYS Alumni
Sarada Thanikachalam, 2010 KEYS Alumni

2015 Intern Award Ceremony
**Mana Abdi - Pima County JTED Intern**

**The Search for the Discovery of a GroEL Targeted Antibiotic**

GroEL, a representative of the E. coli chaperonin system; a member of the Heat Shock Protein 60 family is essential for bacterial survival. GroEL helps with refolding of newly translated and misfolded proteins, inhibition of which can lead to bacterial death. *In vitro* studies have shown that 50% of proteins interact with GroEL when denatured; 30% of these proteins are unable to fold in the absence of GroEL. Previous research screened 700,000 compounds, about 50 of which inhibited GroEL, but were not bactericidal. The Chapman lab previously screened 2000 natural product extracts and 200 pure compounds yielding about 15 biochemical hits, 2 of which were functional in a cell growth assay. Here we report progress towards discovery of a molecule that kills bacteria through inhibition of GroEL.

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**Khalid Ahmad - UA College of Engineering Intern**

**Analysis of Peripapillary Sclera Using Ocugimbal-aided Multiphoton Microscopy**

Primary open angle glaucoma (POAG) disproportionately affects individuals of African descent and Hispanic ethnicity, and, in every major study of POAG including individuals of African descent; African descent was shown to be a significant risk factor for the disease. Various methods are used to identify baseline differences in microstructure and mechanical properties in the posterior sclera of human donors, to develop a better working model of what affects chances of developing POAG. The purpose of this experiment was to use an Ocugimbal to accurately image the peripapillary sclera (PS) of ocular tissue, and to determine its potential application in imaging these tissues to outline differences in the biomechanical environment of human ocular tissues as a function of age and ethnicity.

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**Mariam Alam - Sanofi Intern**

**Upregulation of Nrf2 by TSC22D4 confers chemoresistance to Medroxyprogesteroneacetate (MPA) in Type 1 Endometrial Carcinoma**

Nuclear factor erythroid-derived 2-like-2 (Nrf2) is a redox sensitive cytoprotective transcription factor that protects normal and cancerous cells. Certain cancers upregulate Nrf2 through both known and unknown mechanisms leading to enhanced cancer cell survival. Nrf2 is essential to cancer research because lowering levels may reduce cancer risk. Here, TGFβ-stimulated clone 22 Domain family 4 (TSC22D4) has been shown to upregulate Nrf2, allowing endometrial cancerous cells to acquire chemoresistance to progesterone, the standard hormonal therapy. We hypothesized that Nrf2 levels accumulate due to TSC22D4 induction by progesterone treatment, giving rise to AKR1C1 induction, a target gene of Nrf2. Ultimately, the results support that induction of AKR1C1 is responsible for progesterone metabolism and causes endometrial cancer cells to develop chemoresistance to progesterone.
The Effect of Zinc in Rhodopsin Activation

More than 40% of the pharmaceuticals target G-protein-coupled receptors (GPCRs). The activation of visual GPCR, rhodopsin, leads to an equilibrium between inactive Meta-I and active Meta-II states. Metal ions such as zinc influence GPCR function by allosterically binding to the protein as observed in the cases of Alzheimer’s and Parkinson’s disease. How Zn$^{2+}$ affects the rhodopsin photoactivation was investigated using electronic spectroscopy. We hypothesized that inactive Meta-I is stabilized by Zn$^{2+}$ by allosterically binding to the protein. We found that the active Meta-II is destabilized by Zn$^{2+}$, and the equilibrium between Meta-I and Meta-II is shifted towards inactive Meta-I. Further experiments will be conducted to understand the effect of zinc on rhodopsin-transducin interaction. This study will aid the pharmaceutical field to develop improved molecular drugs.

Enhanced Follicle Competition in Aedes aegypti Mosquito Ovaries by Partial Blood Feeding

Mosquito ovary is an ideal model for studying mechanisms involved in apoptosis of primary follicles since the follicle development is tightly regulated by blood feeding. Follicle apoptosis is an important physiological adaptation by mosquitoes to maximize the number of synchronously developing follicles and directly contribute to an overall reproductive performance by allocating available resource for other cohort follicles. The objective of the present study was to analyze the effect of dietary protein level on mosquito reproductive fitness by examining fecundity, viability, and phenotypes present in the ovary. Female mosquitoes that fed fully show significantly higher fecundity than those fed partially, indicating that the latter shows significantly higher follicle competition. The distribution and occurrence of caspase positive follicles was also determined.

The effect of pre-recorded urban environmental noise on weight gain and feeding is species-dependent

Rodent models are needed to develop treatments to improve poor health caused by sleep deprivation in humans. This study’s purpose was to determine if environmental noise increased weight gain and hyperphagia in mice as previously seen in rats, increased orexin mRNA and peptide levels, and validated noise levels inside the mouse cage. We hypothesized that noise-exposed mice would have greater weight gain due to increased food intake, elevated orexin levels and that the volume of the noise would be the same inside and outside the mouse box. However, noise-exposed mice had similar total weight gain, total food intake and spillage compared to non-sleep deprived mice. Noise volume was significantly less inside the box (mean 12db). Response to pre-recorded environmental noise differs between mice and rats.
Parameterization of *ex vivo* porcine kidneys as a measurement of renal viability

As the increased prevalence of diabetes results in more reports of kidney failure, the demand for viable donor kidneys continues to increase. Magnetic Resonance Imaging (MRI) presents a method of measuring kidney perfusion that can help determine kidney viability. *Ex vivo* porcine kidneys were imaged using a 3.0 T MRI scanner. Kidneys were compared at different temperatures and persufflation levels using dynamic Gadolinium-enhanced images to examine perfusion throughout the cortex. Both sets of conditions were shown to be differentiable by two parameters: (1) maximum cortex value and, (2) slope after maximum cortex value. High temperature and persufflated kidneys were found to be more responsive than their counterparts. MRI may present a new method of more accurately determining kidney viability.

Comparing the nutritional value of *Datura discolor* and *D. wrightii* on growth performance of the *Manduca sexta*

Previous studies have shown that *Manduca sexta* moths prefer the host plant *Datura wrightii* over *D. discolor*, implying a nutritional benefit to larvae. The amount of leaf material eaten and growth stage of each individual were recorded daily. Larvae were reared on both host plants. Once a larva reached the 4th instar, it was immediately put in the freezer, dried and its dry mass recorded. Larval mass, number of days required to reach the 4th instar, and total leaf area ingested were used to compare growth performance and nutritional value of the two species of *Datura*. Growth performance was predicted to be higher on the preferred *D. wrightii* diet. However, there was no significant difference in growth performance between *D. wrightii* and *D. discolor*.

Synergistic effects of garlic derived natural compounds with Gemcitabine in Pancreatic Ductal Adenocarcinoma

Pancreatic ductal Adenocarcinoma (PDAC) avoids modern treatments with chemotherapeutic agents through its intrinsic resistance mechanisms. Nonetheless, previous studies have shown the anti-cancer effects of Gemcitabine and garlic derived products. Gemcitabine paired with a range of disulfide compounds, has been shown to have a greater efficacy than Gemcitabine alone. Our results showed that disulfiram, and PX-12, in synergy with Gemcitabine, increased the levels of gamma-H2AX by a significant margin, indicating DNA double strand breakage, which, in turn, leads to apoptotic death. In our initial screening, Gemcitabine paired with the disulfide compounds, proved to have a positive synergy, indicating some variety of DNA damage, and cell cycle arrest. Our study suggests that the combination of Gemcitabine and organosulfur compounds can produce anti-proliferative effects against various types of cancer.
**Poster Abstracts**

**Kayla Cordero - Hillman Trust Intern**

**Product Performance of the Marketed Inhalers ProAir®, Proventil HFA, and Ventolin**

My lab focuses on product performance testing of different types of inhalers, comparing particle size, dose, and the amount of drug delivered. All marketed inhalers claim they give a dose of 108 μg of albuterol sulfate per actuation; however, all inhalers do not give that exact dose. This may be the result of drug deposition in any part of the respiratory system before it can be delivered to the lungs. Product performance testing is executed with an aerodynamic particle sizer and an impactor inlet, to quantify the dose of albuterol sulfate that makes it to the lungs compared the drug that is deposited before the lungs. It was found that, of three marketed products, ProAir® was the closest to the prescribed dose, while being the most consistent.

**Reuben Dayzie - Hillman Trust Intern**

**Finding the Expression of CLAVATA1 and CORYNE in Arabidopsis Using Marker Analysis**

This research determined the expression profile of CORYNE (CRN) and CLAVATA1 (CLV1) in Arabidopsis root. CRN and CLV1, receptor-like kinases located in the cell membrane, are responsible for the growth and development of the primary root as well as the shoot apical meristem. Two lines were studied for CRN (CRN::GUS 8 & CRN::GUS 29) and two for CLV1 (pCLV1::GUS J3-T4 & pCLV1::GUS WT2). We treated roots with X-GLUC to visualize β-glucuronidase (GUS) and locate CRN or CLV1 expression within the root. Results showed that CRN and CLV1 were found in the stele, the quiescent center, the leaves (CLV1 only), and in lateral root primordia (CRN only). The CRN and CLV1 lines were also treated with CLE19 peptide to see if this would cause a change in expression.

**Faith Digby - Thomas and Reenie Keating Intern**

**Are women superior to men......with regards to cellular response to intermittent hypoxia?**

Intermittent hypoxia is repetitive episodes of reduction in tissue oxygen levels (hypoxia) that occurs in a common clinical condition called obstructive sleep apnea (OSA). OSA has been associated with cardiovascular mortality, and such an association is stronger in men than in women. The mechanisms underlying such sex differences are unknown, but inflammation has been suggested as a mechanism underlying the cardiovascular effects of OSA. We aimed to determine sex differences in pro-inflammatory cytokine production by peripheral blood mononuclear cells (PBMCs) in response to in-vitro intermittent hypoxia. We found that PBMCs derived from men produced more interleukin-6 than that in women. Sex differences in cellular response to intermittent hypoxia may explain the association between OSA and cardiovascular mortality.
**Poster Abstracts**

**Aria Fodness - BIOS Institute Intern**

*Toxoplasma gondii infection alters size of cells in central nervous system*

The parasite *Toxoplasma gondii* creates parasite-filled cysts within cells of the CNS (central nervous system) and is estimated to affect about 60 million people in the US alone. We used Imaris image analysis software to determine the volume and surface area of neurons and astrocytes in infected and uninfected mice. Astrocytes are larger in infected mice, while neurons in uninfected mice are larger than those, which have interacted with *Toxoplasma* in infected mice. These findings show that chronic infection with *Toxoplasma gondii* alters the size of CNS cells.

**Abigail Foley - Anonymous Intern**

*RECEPTOR-LIKE PROTEIN KINASE 1 and CLAVATA2 Regulate Root Growth in Arabidopsis thaliana*

*Arabidopsis thaliana* receptor-like kinases participate in signaling pathways that regulate proliferation and differentiation. Redundant functions complicate the process of delineating their mechanisms; phenotypic readouts are often masked. To clarify previous findings, we measured root lengths of *Arabidopsis thaliana* single and double mutants of *RECEPTOR-LIKE PROTEIN KINASE 1* (*RPK1*) and *CLAVATA2* (*CLV2*) with comparison to wild-type (Colombia ecotype), under both untreated and CLAVATA3/Endosperm Surrounding Region (ESR)-related CLE19 peptide treated conditions. Deviation in mutant root lengths from wild-type indicates *RPK1* and *CLV2* are involved together in regulatory processes leading to development of the mature root.

**Nathaniel Gallegos - Thomas R. Brown Family Foundation Intern**

*Retinal Neuron Dysfunction in Diabetes*

A prominent complication of diabetes is the loss of visual functions. This is caused by diabetic retinopathy, which is clinically defined as the addition of new, defective blood vessels that leak and cause damage to the eye. However, previous electroretinogram studies have shown that there are retinal neuronal signaling differences occurring prior to the retinopathy. Single cell recordings of retinal cells were taken to compare signals from control and diabetic mice. Our results show that there is an imbalance in electrical activity of retinal neurons in diabetic mouse cells when compared to normal cells. In order to have optimal visual functions, the excitatory and inhibitory signals need to be in equilibrium. This correlates with the decline in visual functions seen in diabetic patients.
**Poster Abstracts**

**Smita Gopalakrishnan** - Anonymous Intern

**PI** - Dr. Danielle Zarnescu

**Screening for neuroprotective compounds in a Drosophila model of ALS based on TDP-43**

Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disease that has no cure. The RNA/DNA binding protein TDP-43 has been implicated in ALS both as a marker of pathology and as a causative factor. We performed a drug screen for novel compounds that improved locomotor function in a Drosophila melanogaster (fruit fly) model of ALS that recapitulates several aspects of the disease. Larvae expressing human wild-type (TDP^WT) or mutant TDP-43 (TDP^G285S) and controls (w^1118) were raised on fly food containing different drugs and compared through larval turning. Faster larval turning times indicated a rescue in the phenotype. Of the compounds screened, one drug showed significant improvement for TDP^WT larvae, showing that the drug may have the potential to improve locomotor dysfunction in ALS patients.

**Nizar Hadeli** - Thomas and Reenie Keating Intern

**PI** - Dr. Julie Ledford

**The effects of Body Mass Index (BMI) and asthma on tissue eosinophilia and surfactant protein-A levels in human lungs**

Eosinophils are white blood cells that aid in immune response, but prove to be harmful in excess in the lung. Surfactant protein-A, or SP-A, is a protein component of surfactant, which helps regulate immunological response, and behaves as a chemoattractant, pulling eosinophils from the lung tissue and into the airway. Differences in Body Mass Index (BMI) are speculated to impact SP-A levels in the lung, yielding differences in eosinophil concentration. Under the mentorship of Dr. Ledford, I used immunohistochemistry to visualize eosinophils, and western blot analysis to determine SP-A concentrations in human lavage fluid. Our findings reveal relationships between SP-A and tissue eosinophilia. This preliminary data will be useful in paving the path for future research in this field.

**Saba Hagiri** - BIOS Institute Intern

**PI** - Dr. Jill Tardiff

**Characterization of the Sarcoplasmic Reticulum Calcium Uptake in Transgenic Mice**

Hypertrophic cardiomyopathy (HCM) is a disease that affects 1/500 Americans and causes the myocardium to become abnormally thick, leading to heart failure. Mutations of sarcomeric proteins, the fundamental unit of cardiac contraction, are associated with HCM. The mutation of the cardiac protein troponin T (TnT R92L) was studied. In addition, it has been shown that CamKII aids in the storage of calcium in the sarcoplasmic reticulum (SR) by phosphorylating a regulatory protein on the SR, phospholamban (PLB), removing the “brakes” on calcium uptake. By crossing two transgenic mice, one expressing 50% R92L and one expressing 40% AC3I, a CamKII inhibitor, a comparison of the effect of the R92L genotype compared vs. R92L x AC3I genotype on CamKII activity was determined via a calcium uptake assay and Western Blotting.


**Poster Abstracts**

**Raynisha Jewelryman**

**Does Reduced Workload Cause Inactivity in *Temnothorax rugatulus* Ants?**

Ant colonies are very productive, though do colonies become inactive to save energy if there is less work to be done? It may be that the inactive workers in ant colonies do not have work to perform and are therefore saving energy. I hypothesize that experimentally reducing offspring in the nest would lead to reduced activity. We therefore collected *Temnothorax rugatulus* from Mt. Lemmon in Tucson, Arizona and painted individuals in these colonies for behavioral analysis. We used general linear mixed models to analyze inactive behavior and concluded that the brood manipulation did not significantly change the amount of inactivity in ant nests (p > 0.05).

**AJ Johnson - Thomas R. Brown Family Foundation Intern**

**Effect of Temperature and Inoculum on Steinernema ‘Licanray’ Sex Ratio of First Generation Adults**

Insects are everywhere, an integral part of any ecosystem. However, some insects have a negative impact on human life, by destroying agricultural crops or invading people’s homes. Entomopathogenic nematodes are a natural alternative for insect control. Nematodes are simple round worms that parasitize and kill insects. Nematodes of the genus Steinernema have a symbiotic relationship with the enterobacteria, Xenorhabdus. When infective juvenile (IJ) nematodes penetrate the insect, the nematode will release the bacteria killing the insect. The nematodes then mate and reproduce. This study aimed to determine how the sex ratios differ between three different temperatures of culture (15°C, 20°C, 30°C) while using different inoculums (10 and 100 IJ/ml) of nematodes. Sex ratio determination will help understand how nematodes can be applied more efficiently to control insect pests.

**Martha Kiela - Thomas and Reenie Keating Intern**

**CNS Immune Response Differences With Distinct Strains of *Toxoplasma gondii***

*Toxoplasma gondii* is an intracellular parasite that can cause brain disease ranging from mild to severe in the immunocompromised and the developing fetus. Though the determinants of disease severity are not well understood, recent data suggest that the genotype of the infecting *Toxoplasma* strain influences clinical outcomes. To understand these strain-associated differences in outcomes, we are studying the brain immune response provoked by two genetically divergent *Toxoplasma* strains (Type II and Type III). Our preliminary results indicate that Type II parasites provoke a stronger T-cell response, while Type III parasites elicit a macrophage-dominant response in the brain. Currently, we are using the F1 progeny from a Type II x Type III cross to identify the parasite factors linked to these differences in the neuroinflammatory response.
**Poster Abstracts**

**Alex Lehamn - SWEHSC/UA College of Pharmacy Intern**  
**PI - Dr. Eli Chapman**

**Discovery of natural product antibiotics that target GroEL**

Chaperone proteins function in a critical role of maintaining proteostasis by assisting misfolded proteins to fold into their native form after initial translation or cellular distress. This study seeks to find inhibitors of the GroEL/GroES chaperonin system, the only chaperone system that is essential for bacterial life in all conditions. Consequently, the discovery of an inhibitor of this protein could yield a novel antimicrobial mechanism to treat bacterial diseases and infections. A malachite green assay was used to conduct a biochemical screen of approximately 1,300 natural product extracts. Twelve compounds were found to inhibit the ATPase activity of GroEL by more than 45%. Further work will involve the optimization of the biological activity of these extracts.

**Alexus Knight - Connie Hillman Family Foundation Intern**  
**PI - Dr. Sean Limesand**

**Identify the Differentiation Process in Cultured Neonatal Porcine Islet-like Clusters**

This project’s main objective was to determine if differentiation occurs in neonatal porcine islets. Porcine islets provide a suitable cell based treatment to replace insulin in Type 1 Diabetes patients. Immunohistochemistry was performed on cultured neonatal porcine islet-like clusters to define progenitor cells that acquire a mature beta cell phenotype and express insulin. Morphometric analysis on neonatal porcine islets demonstrates beta cells differentiation from the progenitor epithelium. In addition, beta cells co-express vimentin, a mesenchymal marker, which indicates that these newly formed cells migrate from the epithelium through an epithelial-mesenchymal transition (EMT) process. These critical processes were previously described in the developing pancreas and may provide avenues to increase beta cell mass in cultured neonatal porcine islets.

**Aradhana Kumar - SWEHSC/UA College of Pharmacy Intern**  
**PI - Dr. Serrine Lau**

**The Contribution of Cellular Stress Proteins in Mediating All-Trans Retinoic Acid Cytoprotection Against Renal Cellular Injury**

Chemical-induced nephrotoxicity is a major cause of acute kidney injury. Pretreatment of LLC-PK1 cells with all-trans-retinoic acid (ATRA) affords cytoprotection against $p$-aminophenol (PAP), iodoacetamide (IDAM) and 2-(glutathion-S-yl)hydroquinone (MGHQ)-induced necrosis. To investigate the mechanism(s) by which ATRA affords cytoprotection, its effects on the stress protein $p$-ERK and its target gene CyclinD1 were analyzed using western blotting. A two-fold induction was seen early at 2 hr but returned to baseline by 8 hr. The first step in transitioning to human cells is a PAP dose response experiment analyzed by the MTS cell viability assay. The doses that gave a 50% reduction in viability were 200 and 300 µM for HKC8 and HKC11, respectively. Thus, ATRA may serve as a therapeutic intervention in acute kidney injury.
**Ivan Lu** - BIO5 Institute Intern

**PI - Dr. David Armstrong**

**Combined use of platelet-rich plasma, bilayered acellular matrix grafting, and negative pressure wound therapy in the targeted surgical treatment for acute severe diabetic foot disease**

A new technology for diabetic wound treatment, Platelet-Rich Plasma (PRP) has become very popular in the recent years. PRP secretes growth factors that can promote granulation, local wound inflammation control, and, the latest research suggests, that PRP also has an antibiotic-like effect. For three weeks, Bilayered Acellular Wound Matrix Grafting (BAMWG) and Negative Pressure Wound Therapy (NPWT) are applied as treatment. This time window is a critical period of wound prognosis: if the infection worsens or proliferates, amputation is required. Contrastingly, if the infection is controlled, treatment may be continued and limb salvaging can be achieved. This study shows that when these primary treatment technologies are combined the healing of the patient is promoted. Ultimately, when implemented correctly, this treatment process allows for an alternative to amputation.

**Jacob Mapp** - BIO5 Institute Intern

**PI - Dr. Craig Aspinwall**

**Stabilization of Black Lipid Membranes for Biosensor Creation**

Black Lipid Membranes (BLMs), synthetic mimics of the cell membrane, could potentially be used as the basis of a biosensor used for rapid screening of diseases. We inserted ion-channels to detect various proteins associated with a plethora of diseases. We first stabilized the BLMs, as they last less than four hours, by adding butyl-methacrylate (BMA) and Ethylene Glycol Dimethacrylate (EGDMA) monomers to strengthen the bi-layer the lipids form. To test the effectiveness of the monomers, we suspended the lipids across the aperture of a pipette tip and measured the mV it took to breakdown the bi-layers. We compared the non-doped lipids to the monomer-doped lipids after zero, five, and ten minute polymerizations. Polymerization effectively strengthened the lipid bi-layer as hypothesized.

**Danielle Mara** - Thomas and Reenie Keating Intern

**PI - Dr. Wulfla Gronenburg**

**Associative learning in Aphaeogaster cockerelli ants through olfactory classical conditioning**

Associative learning has been studied in many vertebrates and invertebrates. Since the 1950s, the proboscis extension response for such learning has been used in social insects such as honeybees. However, a similar conditioning sequence has not been established for ants, which are also advanced social insects. Here, I presented a conditioning protocol using Aphaenogaster cockerelli ants. When the antennae of ants are stimulated with sucrose, the ant extends its tongue to feed, termed here a ‘tongue extension response’ (TER). TER is conditioned by pairing an odor with sucrose. About 30% of the ants learned the association within 10 trials, displaying the TER without the presence of sucrose. The results suggest that additional learning trials may result in more ants learning the association.
Analyzing the Intrinsic Permeability of the Posterior Sclera and the Retina-Bruch’s-Choroid Complex

Glaucoma is a progressive ocular disease that leads to visual loss and is the second leading cause of blindness worldwide. Research in the field of ocular biomechanics has shown that the deformations of the optic nerve head (ONH) leads to retinal ganglion cell death through axonal insult. The disease has also shown itself to affect different racial groups disproportionately, with African Americans being affected the most. To understand why Glaucoma rates are higher in certain racial groups it is important to characterize differences in the biomechanical environment of each group. Identifying the permeability of the sclera and Retina-Bruch’s-Choroid Complex (RBC) may elucidate the role it plays in glaucoma. The aim of the study was to investigate different methods to experimentally determine permeability.
**Creating an in vitro model of NASH associated changes in drug metabolism and disposition**

Nonalcoholic Steatohepatitis (NASH) is a form of liver disease affecting 17% of adults in the United States. NASH in humans leads to dysfunction in liver drug transporters and metabolism enzymes, which may result in drug toxicity. It is known that drug transporter and metabolism enzyme expression will decrease similarly in rodent NASH models. Data collected from western blots showed that rodent livers with NASH have decreased expression of transporters and metabolism enzymes which reinforces previous research in the Cherrington lab showing a decrease in expression of drug uptake transporters and metabolism enzymes in rodent NASH models. Future studies will treat primary rodent hepatocytes with stearic acid and iron in order to recapitulate NASH and observe the effects on liver transporters and metabolism enzymes.

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**Conservation of gene regulatory networks in insect appendage development**

Insects are known for the amazing diversity of their appendages. To understand the evolutionary origins of this diversity, we proposed to see whether genes that pattern the appendages in the model organism *Drosophila* have the same or different functions in another insect, the flour beetle *Tribolium castaneum*. We began to test the function of the four jointed, Dachsous and fat genes in appendage development in *Tribolium castaneum*. Mutations in all of these genes in *Drosophila* effect the size and shape of the appendages. We successfully amplified both Fat and Dachsous clones using PCR. We made double-stranded RNA of the four-jointed gene and tested its function by injecting dsRNA into both early embryos and larvae. The outcome of the RNAi experiments are pending.

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**Effects of Radiation Treatment on Keratin 5 Progenitor cells in Salivary Glands**

The Limesand lab studies salivary gland stem/progenitor cells, as they are an attractive alternative for developing therapies to restore salivary function, dry mouth, lack of nutrition, and a higher risk of developing cavities. We previously demonstrated that EdU+ cells comprise a heterogeneous population of progenitor cells (Keratin5, Keratin14, cKIT). We developed a label-retaining assay with EdU to trace long-lived quiescent cells in mouse salivary glands. In this study, we focused on the Keratin 5 population, using immunofluorescent staining of formalin fixed paraffin-embedded tissue in salivary gland sections. This lab’s previous research demonstrated that the number of EdU cells was unchanged following radiation, yet function was not restored. Our hypothesis was that the stem/progenitor cells were not differentiating correctly upon radiation treatment, thus failing to restore damage.
Abhijay Murgesan - Thomas R. Brown Family Foundation Intern  
PI - Dr. Wulfilia Gronenberg

Measuring Metabolic Activity of the Antennal Lobes and Mushroom Bodies of *Aphaenogaster cockerelli* Ant Brains Using Cytochrome Oxidase Histochemistry

This research aimed to measure the level of metabolic activity in the brains of *Aphaenogaster cockerelli* ants to study if underlying differences in metabolic activity across structures of the ant brains are associated with learning capability. The work attempted to determine if there were correlations between the ants’ memories/abilities to learn and activity levels of the antennal lobes and mushroom bodies within the brain. Cytochrome oxidase (CO) histochemistry techniques were used to stain the brain sections, and then ImageJ software was used to analyze photographs and quantify the metabolic activity. T-tests were used to determine if differences were statistically significant or not. In addition, the study hoped to establish the legitimacy of CO histochemistry as a procedure in studying neuronal activity in ants.

Anuja Oke  
PI - Dr. Danzou Yang

C-myc Promoter Region: Survey of Inter- and Intra-species Control Elements

Specific genetic elements in the promoter regions of cancer-causing genes can control the quantity of expressed protein. One such element, the G-quadruplex, a DNA secondary structure formed in a guanine-rich promoter region, decreases protein expression of c-myc and can be targeted for cancer therapeutics. c-myc is an oncogenic transcription factor whose overexpression can lead to the unregulated expression of many downstream genes. Changes within and between species in promoter elements of c-myc were identified to reveal the potential G-quadruplex formation, providing mechanistic insight into transcriptional control. Factors that specifically affect the G-quadruplex region, such as binding sites and control elements, were identified by aligning different species' sequences, as well as intra-species variations within the human gene.

Raj Patel - UA College of Medicine Intern  
PI - Dr. Heidi Mansour

Characterization of Spray Dried Nano/Microparticulate Drugs

It is important to characterize the physicochemical properties of dry powder (drug) formulations as they influence aerosol performance, stability, bioavailability, and processing during manufacturing. This research project’s aim is to design and characterize a novel nano/microparticulate dry powder inhaler to treat asthma and chronic obstructive pulmonary disease. In this study, the nano/microparticles were created through advanced spray drying particle engineering technology using a novel, experimental drug and a non-reducing sugar, D-mannitol. To confirm and analyze both drugs for these select characteristics we had used methods such as Differential Scanning Calorimetry (DSC) which determined phase behavior and phase transitions, Karl Fischer Titration (KFT) which determined the residual water content, and Hot Stage Microscopy (HSM) which helped confirm and image the thermal behaviors such as melting points, boiling points, and sublimation.
**Poster Abstracts**

**Bassil Ramadan - SWEHSC/UA College of Pharmacy Intern**

**PI - Dr. Terrence Monks**

**Mutated in Colorectal Cancer (MCC) is a new Keap1-interacting protein**

Mutated in Colorectal Cancer (MCC) is a protein that was thought to be the cause of familial colon cancer; however, it was later found to be mutated only in some colorectal tumors. MCC is actually a potential tumor suppressor as it blocks cell cycle progression, helps in differentiation, inhibits migration, and helps in DNA repair. In this study, the role of MCC in the activation of the protective Nrf2 pathway was investigated. MCC was found to interact with Keap1, a protein that normally restrains Nrf2 from moving to the nucleus and transcribing for a variety of proteins. MCC’s association with Keap1 slightly increased the protein expression of Nrf2 in the cytoplasm and the nucleus, although no activation of Nrf2 downstream genes was identified.

**Bianca Reilly - SWEHSC/UA College of Pharmacy Intern**

**PI - Dr. Donna Zhang**

**Dopamine and Arsenic Disrupt Alpha-Synuclein Homeostasis in Parkinson’s Disease**

Parkinson’s Disease (PD) is the second most common neurodegenerative disorder. The loss of dopaminergic neurons in the Substantia Nigra Pars Compacta, which play a major role in modulation of fine movement and cognition, is the major contributor to disease progression. The molecular mechanisms underlying idiopathic PD are poorly understood; however, dopamine (DA), and alpha-synuclein (SYN) play a central role in PD development. In order to pinpoint the interaction between SYN and DA, DA thioether conjugates have been synthesized and shown to inhibit the crosslinking of SYN molecules. In addition, the effects of environmental arsenic exposure on PD progression has been studied in vitro and in vivo. The results are discussed.

**Lisa Robbins - Sanofi Intern**

**PI - Dr. Paloma Beamer**

**Determining the most effective method of removing soil from hands for use in risk assessment**

This study tested two methods of soil extraction from the hands to determine the most effective cleaning method: “Hand Wipe” or “Hand Wash”. The most accurate method of hand soil extraction will be used to determine the amount of soil a person contacts daily. We preferred the Hand Wash method because the Hand Wipe method was not feasible. Once daily contact with soil is determined, the soil will be tested for contaminants to identify those that may cause illnesses. The amount of soil and the frequency of contact with soil will help define the amount of harmful contaminants contacted daily. Future research will determine how to decrease the number of effected people and lower the risk of diseases from contact with contaminated soils.
Accumulation of a marker foreign protein in seeds of *Camelina sativa* with various genetic backgrounds

With increasing population and decreasing amount of arable land, more nutrients need to be obtained from crops. *Camelina sativa*, a dicotyledonous winter growing crop, is an ideal model for genetic modification and production of transgenic products. This project involved transforming three lines of Camelina (non-transgenic, β-carotene, and β-carotene RNAi storage protein) to increase foreign protein content using a GFP-kdel reporter. Suppression of a major storage protein and/or the use of the nutraceutical carotenoid β-carotene may increase seed proteome in Camelina. A seed specific promoter expressing GFP was used to assess the amount of introduced protein in seeds. Using these genetic backgrounds, Camelina is expected to have more protein accumulation in the β-carotene RNAi storage protein line, as previous work has shown with soybean.

The impact of increased insulin signaling in the *Anopheles stephensi* midgut on immunity, lifespan, and reproduction

Malaria is one of the world’s most prevalent diseases. There are an estimated 660,000 deaths due to malaria each year. Despite efforts to control malaria, the appearance of insecticide-resistant mosquitoes and drug-resistant parasites continues to accelerate worldwide. Therefore, there is an urgent need for innovative strategies to ease this burden. One strategy is to genetically engineer better-fit mosquitoes that are less parasite-susceptible to replace the wild population. In mosquitoes, the insulin/insulin growth factor 1 signaling (IIS) cascade regulates lifespan, reproduction, and innate immunity. In this study, we genetically engineered transgenic *Anopheles stephensi* mosquitoes to over-express an active form of *A. stephensi* MKP4 (AnsteMKP4), part of the IIS pathway. Future studies will focus on how MKP4 affects the reproduction and lifespan of transgenic mosquitoes.

Does Extra Work Activate Lazy Individuals in *Temnothorax rugatulus* Ants?

The *Temnothorax regulus* ant colony works as a group under one queen not one boss. These ants solve problems by using distributed solutions in a strategy that humans do not fully understand yet. We know that the strategies they use are extremely productive as ants are highly diverse and abundant. If ants are so successful why is there laziness in ants and how does it contribute to the colony? I used brood manipulation to test if inactive ants are reserves in case the demand for brood care outstrips the typical amount of work. I collected colonies on Mt. Lemmon, AZ, and used behavioral analysis to determine that increased brood does not activate inactive individuals. Therefore lazy ants do not seem to be a reserve workforce.
Examining Mutational Status of Histone Acetyltransferases in Diffuse Large B-Cell Lymphoma

Diffuse Large B-Cell Lymphoma (DLBCL) is an aggressive, heterozygous cancer. While the current treatment, Rituximab-CHOP Chemotherapy, has prolonged survival, 30% of patients relapse, indicating resistance and cancer progression. A class of drugs, known as Histone Deacetylase Inhibitors, shows promise as a therapeutic by regulating the cycle of acetylation and deacetylation. To understand why some cell lines are resistant, genes that code for Histone Acetyltransferases (HATs) were examined. Specifically, the HAT domain of the CREB Binding Protein (CREBBP) was sequenced and its expression levels were studied in sensitive and resistant cell lines to find missense mutations that may be correlated with resistance. Since a deficiency in acetylation may inhibit key tumor suppressors, understanding the mutational status of HATs is necessary in creating drug therapies that will cure all DLBCL.

Computational Analysis of the Rb-E2F Bistable Region

The reactivation of quiescent cells (e.g. stem cells) into proliferation is initially controlled by the bistable Rb-E2F gene pathway. The bistable nature of the Rb-E2F pathway means that a cell exists in one of two states: E2F-ON (proliferation) or E2F-OFF (quiescence). In 2008, Yao et al. derived a mathematical model for the Rb-E2F pathway. Using the computer program COPASI, parameters in the Yao model were mutated in order to predict the effects that these mutations had on the E2F-activation serum threshold, the E2F-deactivation serum threshold, and the E2F half-activation time. From this, it was possible to categorize mutations in the Rb-E2F pathway based on their effects on the width (the difference between the serum thresholds) and the midpoint (the relative location) of the bistable region.

Photodynamic elimination of skin cancer cells using an endogenous tryptophan photoproduct contained in human skin

Oxidative stress is a key mechanism of skin damage and cancer caused by environmental exposure to solar UV (ultraviolet) radiation. Photo-excitation of endogenous photosensitizers contributes to UV-induced oxidative stress through light-driven (photodynamic) formation of reactive oxygen species. Recently, we identified 6-formylindolo[3,2-b]carbazole (FICZ) as the most potent endogenous photosensitizer in human skin ever described. Here we demonstrate that FICZ can be harnessed for the photodynamic elimination of malignant skin cells. Our experiments indicate that FICZ displays activity as a nanomolar photosensitizer, potentiating UV- and visible light-induced oxidative stress with induction of programmed cell death (apoptosis) in human skin cancer cells. Taken together, our data suggest that endogenous compounds found in human skin can serve as novel photosensitizers for the photodynamic elimination of skin cancer cells.
Jennifer Xiao - Dr. Jennifer Barton Intern

**Studying Toxoplasmosis within the Mouse Brain: Automated Identification and Localization of Parasitic Infections**

Infected around 30-70% of the global human population, *Toxoplasma gondii* is one of the most common zoonotic parasites. It can persist lifelong within neurons and has been shown to influence the genesis of many psychiatric disorders (i.e. Alzheimer’s). Our lab is researching the relationship between parasite infection and location within the mouse brain. To study this relationship, our lab developed an in-house Matlab program to count infected cells in each neuroanatomical structure. The program automatically registers histological images to a brain atlas, and then uses color and size thresholds to identify and count cells. The program offers an automated, rapid solution to manually counting and localizing cells, which are labor intensive. In this project, we developed and improved the automatic registration, sensitivity, and specificity of cell counting.

Jamie Young - Connie Hillman Family Foundation Intern

**Bio-Fortification of Chickpea with pro-vitamin A**

Children in developing nations experience devastating Vitamin A deficiencies that often lead to severe ailments, loss of vision, or even death. Within South Asian countries such as India, over 90% of children below 5 years of age who contract Xerophthalmia, a Vitamin A deficiency disease responsible for vision loss, will die as a result. However, a potential solution is presented through the biological fortification of staple crops to increase nutritional value. India is one of the largest producers and consumers of chickpea, making the crop a quintessential candidate for biological fortification. By introducing a chloroplast-specific bacterial phytoene synthase gene, resulting in the enhanced accumulation of the pro-vitamin A carotenoid β-carotene into chickpea, the nutritional demands of Vitamin A deficient children in India may be addressed.
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KEYS Personnel

Dr. Marti Lindsey
Heather Ingram
Margaret Hardy

Dr. Nadja Anderson
Ben Richmond

KEYS Crew

Daniel Matloff
Austin Brown
Ashley Lykins
Kendall Welliver

Matt Wheeler
Olivia Austin
Taylor Wingfield
Samantha Schuster
KEYS Principal Investigators

Dr. Maria Altbach
Dr. David Armstrong
Dr. Craig Aspinwall
Dr. Paloma Beamer
Dr. Judie Bronstein
Dr. Heddwen Brooks
Dr. Michael Brown
Dr. Eli Chapman
Dr. Nathan Cherrington
Dr. Anna Dornhaus
Dr. Erika Eggers
Dr. Wulfila Gronenberg
Dr. Anita Koshy

Dr. Serrine Lau
Dr. Julie Ledford
Dr. Sean Limesand
Dr. Kirsten Limesand
Dr. Heidi Mansour
Dr. Roger Miesfeld
Dr. Terrence Monks
Dr. Paul Myrdal
Dr. Lisa Nagy
Dr. Aiseng Ooi
Dr. Sai Parthasarathy
Dr. Michael Riehle
Dr. Monica Schmidt

Dr. Catharine Smith
Dr. Patricia Stock
Dr. Daekyu Sun
Dr. Jill Tardiff
Dr. Frans Tax
Dr. Jennifer Teske
Dr. Ted Trouard
Dr. Jonathan Vande Geest
Dr. Georg Wondrak
Dr. Danzou Yang
Dr. Guan Yao
Dr. Danielle Zarnescu
Dr. Donna Zhang

KEYS Mentors

Maria Acosta
Andrew Ambrose
Sumita Acharjee
Kofi Bright
Michael Brown
Carla Cabral
Megan Carver
Alex Chibly
Aram Cholaniams
John Clarke
Melissa Davis
Richard De Armond
Dr. Wuquan Deng
Tarek Eid
Cole Eskridge
Nick Everetts

Dave Francisco
Tomoe Hagio
Bryan Harder
Aaron Havas
Steve Howerton
Lewis Hun
Dr. Jun Iseoe
Stephen Jinga
Rebecca Justiniano
Kelly Karlage
Rebekah Keating
Michael Kerins
Robert Kraft
Vishnu Kumarasamy
Megan Latifzadeh
Sarah Lehman

Gavin Leighton
Nathan Lothrop
Elisa Montserrat Rojo de la Vega Guinea
Johnnie Moore-Dotson
Dennis Pollow
Ryan Rath
Jessica Sapiro
Gordon Smith
Jennifer Teske
Vincent Tso
Rachel Wellington

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KEYS Support Team

Olivia Austin
Richard Austin
Aaron Ball
Dr. Heddwen Brooks

Melanie De Sa
Margaret Hardy
Tom Keating
Dr. Clark Lantz

Dr. Andrew Lettes
Brooke Moreno
Dr. Ted Trouard
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