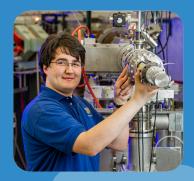
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COLLEGE OF SCIENCE JOINT ANNUAL MEETING





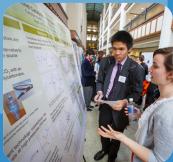












The ninth annual College of Science Joint Annual Meeting (COS-JAM) is part of the eighth annual Undergraduate Scholars Conference. The intent of COS-JAM is to highlight the achievements of undergraduate students conducting research in all disciplines of science.



COLLEGE OF SCIENCE - JOINT ANNUAL MEETING

Schedule and Abstracts Table of Contents

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Schedule - Biological Sciences

Oral Presentations I 1:00 - 2:00 p.m.

Jordan Room 105

Moderator: Dana Barlock

- 1:00 Kyle Cowdrick Reveal3DTM: A Microfluidics Platform for Enabling High-Throughput Characterization of Breast Tumors and the 3D Microenvironment *In Situ*
- 1:15 Eric Donahue Investigating Nephrogenesis through Chemical Genetics: Insights into Peroxisome Proliferator-Activated Receptor (PPAR) Signaling during Zebrafish Kidney Development
- 1:30 Carolyn Hutyra Sustaining viable genetic crosses of *Plasmodium falciparum* through a humanized mouse model
- 1:45 Samantha Piekos Dark-adaptation-mediated rod precursor cell proliferation in the adult zebrafish retina

Poster Presentations 2:30 - 3:30 p.m.

Jordan Galleria

Carolyn Ahlers - APC Regulation of EMP2 Through FAK/Src Signaling

Anne Arnason - APC and MDR1 in chemotherapeutic resistance in breast cancer

Clayton Becker - Inhibition of ADAM10 Stimulates Ganglion Regeneration from Zebrafish Müller Glial Cells

Claire Bedalov - APC selectively mediates response to chemotherapeutic agents in breast cancer Carter Boyd - Detection of Saimiriine Herpesvirus-1 in Saliva, Serum, and Tissue of Captive Bolivian Squirrel Monkeys

Justin Brill - Make no bones without it: Induced mineralization of basicranial osteoblasts under 3D chondrogenic conditions

Caitlin Broderick - Reconstructing the Pre-Settlement Forest of the Yellow River Watershed Amanda Buerger - Modeling linear relationships between Indiana soil composition and tree data Josephine Chau - Implications of salmon-derived nutrients in non-native streams: Investigating the influence of salmon-derived Ca and P in Hunt Creek, Michigan

Sophia Chau - Unlocking global climate adaptation solutions: country resilience index to inform decision-making

Diane Choi - Effect of Spatial Repellents on Dengue Vector Attractancy Behavior

Bonnie Leigh Cruser - Screen to identify *Mycobacterium marinum* strains that are non-cytotoxic to amoeba

Ryan Davila - Creating Environmental Policy for the Great Salt Lake: Effects of ammonia, copper, and lead on brine shrimp (*Artemia franciscana*) mortality from the Great Salt Lake, Utah, U.S.

Nicholas Deason - Outdoor Insecticide-Impregnated Barriers: A New Intervention for Malaria Control in the Solomon Islands

Margaret Dickson - Community Composition of the Burgess and Chengjiang Shales (Drumian and Atdabanian ages of the Cambrian Period)

- Ellen Dowling Exercise During Treatment for Pediatric Oncology Patients: A Retrospective Survey
- Sienna Durbin Antioxidant enzyme-mediated survival of ECM-detached breast cancer cells requires AMPK activation
- Paulina Eberts A fast, recursive normalization algorithm for vignetting correction of large sample montages
- Katia Fernandez Soto APC in Breast Cancer: the ABCs of gene expression
- Megan Fuerst Characterization of Neuropeptide Y Receptor in *Aedes aegypti* Mosquitoes through RNA Interference
- Gary George Photic modulation of Anopheles gambiae mosquito behavior
- Eileen Giglia Hemispheric Equalization of Auditory Responses in Pediatric Single-Sided Deafness
- Alexander Graves Characterizing the expression and function of ADAM17a and ADAM17b in zebrafish retinal development
- Mary Hahm Characterization of ACP Receptors in Anopheles Gambiae and Aedes Aegypti
- Jeffrey Hansen The Effect of Baboon Hybridity on Parasite Resistance Mechanisms
- Julia Hart Linking Decomposition to Methane Production in Alaskan Ponds
- Mallory Hawksworth Characterization of Octopamine G-Protein Coupled Receptors in Anopheles gambiae
- Elizabeth Heilmann Refining a tool to predict antimalarial drug mechanisms of action
- Elisa Herrman Characterizing the Functions of ADAM10a and ADAM10b in Zebrafish Retinal Development
- Sara Hockney Generation, Validation, and Characterization of a pax6b transgenic zebrafish line during retinal development and adult regeneration
- Karen Huang The influence of cover crops on soil health in Shatto Ditch Watershed, IN
- John Huber Calculation of the Serial Interval of Malaria Based on Probabilistic Elements of the Transmission Cycle
- Alex Im A Microwell Cell-Based Assay for the Treatment of Mucopolysaccharidosis IIIA (Sanfilippo Syndrome)
- Jahmel Jordon The Role of EGFR Signaling in Size Homeostasis of *Drosophila* Embryonic Compartments
- Emily Kaye An imbalance between innate and adaptive immune cells at the maternal-fetal interface occurs prior to endotoxin-induced preterm birth
- Sean Keenan Transcriptional Analysis of Polyamine Metabolism in Development and Disease
- Audrey Kelly Regulatory gene expression in the Aedes aegypti retina
- Amanda Kotey An evaluation of the relationship between self-identified race and genetic ancestry
- AnnaKottkamp When is enough, enough? Exploring potential conservation thresholds in an agricultural watershed
- Julia Kruep Periparturient relaxation of immunity in savanna baboons (Papio cynocephalus)
- Dennis Lee Metabolic Transcriptome Shifting of Brain Metastatic Tumors and its Role in Metastatic Success
- Sarah Linesch Data Analysis Pipeline for Studying Cell Signaling in Epithelial Sheets
- Galvin Loughran Regulation of apoptosis and cell competition by hypusination in *Drosophila*
- Gordon MacDougall The Role of p-NF κ B in the Intestinal Epithelium of RAG Knockout and A20 Transgenic Mice

Miranda Madrid - Exploring the effect of climate on the voltinism and phenology of a butterfly hybrid zone using an individual-based simulation model

Zachary Mastrovich - Compatibility of 3D Printed Materials for *In Vivo* Optical Imaging Applications

Shayna McCarthy - Phytoplankton quality influences freshwater lake methanogenesis

Megan McGarel - Fibroblast Oncogenic KRas Expression Induces Lung Epithelial Neoplasia via Enhanced HGF/Met Signaling

Lillian McGill - Use of an ecosystem-based model to predict the effects of non-native Pacific salmon spawning on stream-resident fish in the Great Lakes

Matthew McGoldrick - Multi-material 3D Printing of Multi-segmented X-ray and CT Data Sets of Mice and Rats

Madeline McGovern - Characterization of G-Protein Coupled Receptors in *Anopheles gambiae* and *Aedes aegypti*

Melanie Mironovich - Interaction between the gut microbiome and intestinal parasites in wild baboons

Sneha Modi - Analysis of *Blastocystis* Parasites in *Macaca fascicularis*

James Moley - Potential Mediators of Childhood Exposure to Violence and Health Problems in Young Adulthood

Ashley Murphy - Splenda and Sulci: A Critical Review of the Effects of Artificial Sweeteners on Cognitive and Neural Functioning

Alina Nguyen - Variation in metabolic rate and salinity tolerance within a population of *Daphnia* pulex

Tiffany Nguyen - Elucidating the importance of a nonribosomal peptide synthetase in *Mycobacterium marinum*

Christine Park - Targeting polyamine pathway activity in *Drosophila* Tumorigenesis

Sarah Philo - Increased Calcium Results in Decreased Swarming Motility of the Bacteria Pseudomonas aeruginosa

Stephanie Prince - Anatomical Imaging of Thioacetamide Induced Liver Damage in Mice with Magnetic Resonance

Shella Raja - Aquaponics Across the Spectrum: Bridging Science Education to STEM-Based Careers and Eco-Stewardship

Robert Reed - Bacterial protein half-life analysis

Vincent Riccelli - Bitter and Twisted: Analysis of Diet and Torsional Resistance in the Mandibles of Strepsirrhine Primates

Sarah Rohrman - Temporal Variation of Protozoan Parasites in Singapore Macaque Hosts

David Schipper - A low-cost device to detect amplified DNA for pathogen diagnostics

Lugun Shen - Developing an Effective Immunotoxin that Targets Cells Overexpressing ErbB2

Kaitlyn Simmons - Effects of APC loss on Wnt/β-catenin Signaling in Pancreatic Cancer

Samuel Tadros - Manual annotation of G Protein—Coupled Receptors (GPCRs) in the genomes of *Lutzomyia longipalpis* and *Phlebotomus papatasi*

Denise Tarnowski - Synthesis of N-glycosylated Cetuximab in *Bombyx mori*

Madeleine van Zuylen - Autophagy and Dengue Fever transmission

Zoe Volenec - Climate Change's Effect on Montana's Bunchgrass Prairie

Forrest Weghorst - Combined genetic control of cell body degeneration and axon growth in *Drosophila* photoreceptors

Kourtney Woods - Social status and parasitism in male and female vertebrates: A meta-analysis Helen Zhang - The Role of the mirn23a MicroRNA Cluster in Hematopoiesis and B-Cell Acute Lymphoblastic Leukemia

Oral Presentations II 3:30 - 4:15 p.m.

Jordan Room 105

Moderator: Miranda Madrid

- 3:30 Margaret Dickson The Evolution of Sexual Isolation in the Seed Beetle, *Callosobruchus maculatus* (Coleoptera: Chrysomelidae)
- 3:45 Meagan Hughes The Relationship Between Carbon Nitrogen Ratios and Chlorophyll Levels on the Senescence of Wild Blue Lupine
- 4:00 Michael Spear Environmental DNA detection of the invasive red-eared slider turtle (*Trachemys scripta elegans*)

Schedule - Chemistry and Biochemistry

Oral Presentations I 1:10 - 2:30 p.m.

Jordan Room 101

Moderator: Steven Wietstock

- 1:10 Michael Ahlers Synthesis of Novel GEX1A Analogues: A Potential Lead Towards the Cure of Niemann-Pick Type C Disease
- 1:30 Kevin Hendzel Association Kinetics of Squaraine Pseudorotaxane Formation
- 1:50 Katelyn Virga pH-responsive fluorescent probe for anionic phospholipid sensing at the membrane surface
- 2:10 Anthony Musso Exploring the use of Zn-BDPA's as adjuvants for the cellular uptake of 5-ALA

Poster Presentations 2:30 - 3:30 p.m.

Jordan Galleria

Orrin Belden - Engineering T-cell receptors to optimize anti-tumor immunity

Danielle Boley - Capillary electrophoresis coupled to electrospray ionization-mass spectrometry for metabolomic analysis of tissue extracts

Annalis Cigarroa - Synthetic Routes to New Redox-Active Ligands

Megan Fabry - Localization of ZNF217 and PKM2 in Breast Cancer Cell Lines

Lawrence Gray - pH-responsive fluorescent probe for anionic phospholipid sensing at the membrane surface

William Kasberg - MT1-MMP Affects the Adhesion of Ovarian Cancer Cell Aggregates to Mouse Peritoneal Mesothelium

Megan Kennelly - Synthesis of Dual-Ligand Probe For The Study of Niemann-Pick Type C Disease

Maggie Kerper - Molecular profiling of aggressive breast cancer in a unique patient population from Kenya

Luke Kiefer - Synthesis of UV-Active Cholesterol Mimic for Study of Niemann-Pick Type C Disease

Ivan Leung - Measuring urinary iodine using a paper-based test kit at parts per billion level

Kyle Lewellen - A Novel Method of Relative Tumor Burden Quantification in a Murine Orthotopic Ovarian Cancer Model

Mary McDonald - The Role of PRMT5 in Embryonic Endothelial Development and Angiogensis

Megan McGarel - Matrix Metalloproteinase-3 Impact on Primary Tumor and Metastatic Burden in Aggressive Breast Cancers

Matthew O'Neill - Nickel-Catalyzed Halogen Exchange of Vinyl and Aryl Halides

Kelly O'Shea - Proteins that Determine Destination in RNA Localization

Matthew Onders - Kinetic Study of a Classical Oxygen Atom Transfer Reaction and Characterization of an Unstable Intermediate

Kristal Quispe - Expression of MT1-MMP Affects Epithelial Integrity in Epithelial Ovarian Cancer

Colleen Riordan - Surface-enhanced Raman detection of carbohydrates Anna Sliwinski - Quantification of Side Reactions in SCVcP of A-BIEM and MMA Hyperbranched Polymer

Meredith Vieira - Novel Interactions in the Gephyronic Acid Biosynthetic Pathway and Production of Gephyronic Acid Analogs from Advanced Synthetic Substrates

Emily Zion - Production and biological evaluation of the polyketide naphthocyclinone from the bacteria *Streptomyces arenae*

Oral Presentations II 3:30 - 4:50 p.m.

Jordan Room 101

Moderator: Steve Wiestock

- 3:30 Evan Merryman The Effect of GADD45A-Inducing Drugs in LCC versus RCC
- 3:50 Matthew Messana Regulation of the Oncogene ZNF217 by Localization in Breast Cancer
- 4:10 Kathleen Anthony RNA localization in *Xenopus oocytes*
- 4:30 Maria Moreno Caffaro The Role of Coagulation and Platelet Dysfunction in a Rat Model of Traumatic Brain Injury

Schedule – Mathematics

Oral Presentations I 1:00 - 2:30 p.m.

Jordan 310

Moderator: Jeff Diller

- 1:00 Jacob Haley Coxeter and Artin Group Presentations Arising from Cluster Algebras of Finite Type
- 1:30 Austin Rodgers Distinguishing Sextic Curves Via Syzygies
- 2:00 Xiao Xiao Counting Elliptic Curves with Prescribed Torsion

Poster Presentation Jordan Galleria

2:30 - 3:30 p.m.

Colleen Pinkelman - Sequential Analysis of 2009-2013 American Time Use Survey Data James Schuster and Joseph Germino - Predicting Pitch Outcomes Based on Batter and Pitcher Profiles

Jonathan Vandenburgh - Topological Methods in Data Analysis Yijun Xie - Volatility Estimation and Applications in Stock Options Trading Decisions

Oral Presentations II 3:30 - 5:00 p.m.

Jordan 310

Moderator: Jeff Diller

- 3:30 Jack Burkart Analysis of the Newell-Whitehead Equation
- 4:00 Eric Krakowiak Merton's Portfolio Problem in a Two Asset Economy
- 4:30 David Lenz Representation theory of the Poincare group

Schedule - Physics

Oral Presentations I 1:00 - 2:30 p.m.

Jordan 322

Moderator: Sylwia Ptasinska

- 1:00 William Cantrell A DFT investigation of the anions and neutrals resulting from dissociative electron attachment to thymine
- 1:15 Andrew Jensen Damage to DNA with Various Oxygen levels and Time Constraints by Atmospheric Pressure Plasma Jet
- 1:30 Joanna Kabuye Dissociative Electron Attachment to Dimethylformamide
- 1:45 Emily Kunce Effects of Atmospheric Pressure Plasma on Cytosine Solutions
- 2:00 Justin Skycak Network Motif-Inspired Evolution of Hodgkin-Huxley Neuronal Networks with Spike-Timing Dependent Plasticity

Poster Presentations 2:30 - 3:30 p.m.

Jordan Galleria

Jay Carroll - iLocater: A NIR Doppler Spectrometer

Nicolas Dixneuf - Design of Micro-Pattern Gas Detectors

Patrick Fasano - Modernizing Plunger Control with Low-Cost Digital Electronics

Benjamin Guerin - Measuring the Structure of the Oxygen-16 Nucleus

Louis Jensen - On Carbon-10 Production

Brendan Jones - Surface Sterilization by Cold Atmospheric Pressure Plasma Jet

James Koci - Creating a Vacuum Chamber

William McCormack - Addition of Channels to the Analysis Top-Quark Correlated Higgs Boson Production

James Miller - First AMS Results from the International Atomic Energy Agency's Intercomparison Artifacts

Susan Nace - Analyzing a Supersonic Helium Jet Gas Target for Nuclear Astrophysics

Jason Saroni - Analysis of schematic one-level and two-level nuclear shell models

Trevor Sprouse - A generalized framework for nucleosynthesis calculations

William Wolf - Carbon-14 Graphitization Chemistry

Schedule – Spirit of Science Award Winners

Poster Presentations 2:30 - 3:30 p.m.

Jordan Galleria

Bridget Goodwine - Bridge Length vs Bridge Bend Aidan Kaczanowski - Creating a Programming Language Joseph Rice - Flavorful Memories Maddie Ritchison - Age impact on Stroop Effect Amy Wyse - The Effect of Different Products on Moisture Retention

ABSTRACTS

Oral Presentation

Synthesis of Novel GEX1A Analogues: A Potential Lead Towards the Cure of Niemann-Pick Type C Disease

Michael Ahlers College of Science Chemistry

Jarred Pickering and Eve Granatosky, Dept. of Chemistry and Biochemistry Advisor: Richard Taylor, Dept. of Chemistry and Biochemistry

Niemann-Pick disease Type C (NPC) is a rare and fatal lysosomal storage disease that typically presents before the age of 10¹. Specifically, NPC is characterized by mutations to either the NPC1 or NPC2 proteins that result in defective cholesterol trafficking. Although hydroxypropyl β-cyclodextrin (HPβCD) and histone deacetylase inhibitors (HDACi) such as Trichostatin A are current therapeutic candidates for NPC, there remains no current FDA approved treatment. Our laboratory has recently demonstrated the ability of GEX1A, a type I polyketide natural product isolated from Streptomyces chromofuscus, to restore cholesterol trafficking in NPC1 mutant cell lines. The observed biological activity was of comparable levels to Trichostatin A, yet GEX1A is not an HDACi. In addition, we have observed the ability of GEX1A to restore cholesterol trafficking in HUVECs induced with the NPC phenotype. Thus, the synthesis of GEX1A analogues to be tested in NPC1 and NPC2 mutant cell lines is necessary in order to determine the minimal functionality required for activity against NPC as well as the mechanism of action of GEX1A. Intriguingly, novel anti-cancer natural product pladienolide B shares both structural and biosynthetic similarities with GEX1A. Accordingly, we are currently engaged in the synthesis of an analogue that incorporates the linear side chain of pladienolide B while retaining the western hemisphere of GEX1A (Figure 1). The synthesis is highlighted by novel allylation chemistry² in order to set the requisite stereochemistry at C13 of analogue 1 and C17 of analogue 2.

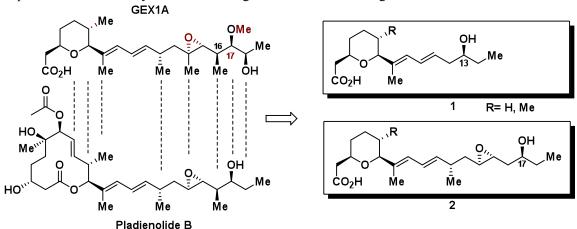


Figure 1. Rationally designed GEX1A analogues 1 and 2 that resemble the linear side chain of pladienolide B.

References

¹Vanier, M. T. Orphanet Journal of Rare Diseases. 2010. 5, 16.

²Suen, L.M.; Steigerwald, M.L.; Leighton, J.L. Chem. Sci., 2013, 4,2413-2417.

APC Regulation of EMP2 Through FAK/Src Signaling

Carolyn Ahlers
College of Science
Science Preprofessional Studies
Alyssa Lesko, Dept. of Biological Sciences

Advisor: Jenifer Prosperi, Indiana University School of Medicine – South Bend, Harper Cancer Research Institute, and Dept. of Biological Sciences

Adenomatous Polyposis Coli (APC) is a large multi-dimensional tumor suppressor that is down-regulated or mutated in many epithelial cancers. APC is widely known to control β-catenin levels via the canonical Wnt signaling pathway; however, it also acts as a scaffold associating with the Dlg and Scrib polarity proteins, microtubules (MTs), and the actin cytoskeleton independently of the Wnt pathway. Our laboratory demonstrated that down-regulation of APC in Madin-Darby Canine Kidney (MDCK) epithelial cells results in loss of apical-basal polarity shown by mislocalization of the gp135 apical marker via immunofluorescence. We also observed a disruption of 3D-morphogenesis resulting in larger, nonspherical and disfigured acini formation. This irregular phenotype was partially restored by the carboxylterminus of APC, containing the binding sites for MTs and polarity proteins. APC knockdown also increased epithelial membrane protein-2 (EMP2), which is up-regulated in multiple tumor types and increases focal adhesion kinase (FAK)/Src signaling. Previous studies from our lab demonstrated that FAK and Src levels are increased in cells isolated from tumors of Apc-mutant mice. Given these findings, we sought to identify whether EMP2 expression could be manipulated by inhibition of FAK/Src signaling in control MDCK cells compared to cells with knockdown of APC in 3D culture. Specific inhibitors include the \(\beta \) integrin inhibitor AllB2, PP2 (Src inhibitor), and a FAK inhibitor. Preliminary data show that inhibiting integrin with AllB2 decreases EMP2 expression in the knockdown cysts. We have also found that migration increases in MDCK shAPC cells and EMP2 levels are altered during migration specifically in the APC knockdown cells. Given the prevalence of APC mutation in epithelial cancers, an understanding of how loss of APC mediates morphogenesis and polarity through EMP2 and FAK/Src signaling will be critical for a more thorough understanding of initiation of tumorigenesis in epithelial cancers.

Oral Presentation

RNA localization in Xenopus oocytes

Kathleen Anthony College of Science Biochemistry

Advisor: Paul Huber, Dept. of Chemistry and Biochemistry

An essential aspect of development is the distribution of maternal information to specific regions of the egg cell prior to fertilization. In Xenopus oocytes, localization of specific mRNAs to either the animal or vegetal hemispheres reflects this cellular polarity. Vg1 mRNA is localized to the vegetal hemisphere, and the 340-nucleotide Vg1 localization element (VLE) is sufficient for proper localization. Six proteins bind directly to the VLE to form a ribonucleoprotein complex that directs localization; however, these six proteins also bind to mRNAs that move to the opposite hemisphere of the oocyte. This observation indicates that other unidentified factors must bind to the ribonucleoprotein complex and determine mRNA destination. To test this hypothesis, I use RNAs that contain the VLE fused to affinity tags, known as aptamers, which enable recovery of ribonucleoprotein complexes that form in vivo. My previous experiments tested three aptamers for specificity of protein binding and efficacy of aptamer recovery, and the tobramycin aptamer RNA seemed the most promising. Thus, tobramycin aptamer RNA was incubated with homogenized oocytes to allow for formation of the ribonucleoprotein (RNP) complex in vitro, the RNA was recovered using the tobramycin matrix, and the bound proteins were identified by mass spectrometry. Due to high levels of nonspecific protein binding, the protein extract was pre-cleared with Sepharose beads and the tobramycin RNA was eluted from the matrix prior to analysis by mass spectrometry. Several proteins involved in RNA localization were identified in the RNP; however, I believe that in vivo experiments will increase specificity of protein binding. My current goal is to microinject oocytes with tobramycin VLE RNA, incubate to allow for formation of the RNP, isolate the RNP from homogenized oocytes using the tobramycin matrix, and identify components of the RNP by mass spectrometry.

APC and MDR1 in chemotherapeutic resistance in breast cancer

Anne Arnason College of Science Science Preprofessional Studies

Advisor: Jenifer Prosperi, Indiana University School of Medicine – South Bend, Harper Cancer Research Institute, and Dept. of Biological Sciences

One in eight women will be diagnosed with breast cancer over the course of her lifetime, making it the most commonly diagnosed cancer in women in the United States. In aggressive breast cancers, cells become resistant to multiple chemotherapeutic agents. ATP binding cassette pumps efflux drugs out of the cell, with Multidrug Resistance 1 Protein (MDR1) being the most commonly studied. Efflux pumps provide an important focal point for targeted chemotherapies, as their expression and function can render many tumors resistant to chemotherapeutic agents. In up to 70% of sporadic breast cancers, the tumor suppressor gene Adenomatous Polyposis Coli (APC) is either mutated or silenced by hypermethylation. These changes in the gene affect a variety of cell processes both dependent and independent of the Wnt/βcatenin pathway. Currently, we are using cell lines derived from tumors in Apc^{Min/+} mice crossed to the Polyoma middle T antigen (PyMT) transgenic model, which are resistant to treatment with doxorubicin and cisplatin. Tumors that arise in the MMTV-PyMT; $Apc^{Min/+}$ mice resemble an aggressive type of triple negative breast cancer. We hypothesized that the cells with Apc mutation will show upregulation in MDR1 expression, which would be enhanced by treatment with doxorubicin, paclitaxel, and cisplatin. Through quantitative PCR analysis, we showed increased expression of MDR1 in cells isolated from tumors of MMTV-PyMT $Apc^{Min/+}$ compared to MMTV-PyMT; $Apc^{+/+}$. We have also demonstrated that mRNA expression of MDR1 further increases in MMTV-PyMT; $Apc^{Min/+}$ cells compared to MMTV-PyMT; Apc^{+/+} cells when treated with doxorubicin and paclitaxel but not cisplatin. We measured the gene expression of ATP-binding cassette sub-family G member 2 (ABCG2), but saw no significant change regardless of treatment. In the future we will validate qPCR results with western blots to confirm protein expression for MDR1 and ABCG2, and look at expression of ABCC2, which is known to efflux cisplatin. Furthermore we plan to determine the activity of MDR1 through calcein incorporation assays as a way to determine the functional impact of MDR1 over-expression. These future studies will allow us to learn more about the mechanisms through which Apc mutation causes chemotherapeutic resistance.

Inhibition of ADAM10 Stimulates Ganglion Regeneration from Zebrafish Müller Glial Cells

Clayton Becker
College of Science
Biological Sciences
Jingling Li, Dept. of Biological Sciences
Advisor: David Hyde, Dept. of Biological Sciences

Degenerative retinal diseases such as retinitis pigmentosa or choroideremia affect millions of people worldwide. Humans do not possess a mechanism for retinal regeneration, but lower vertebrates, such as zebrafish, can regenerate retinal neurons that are lost due to injury. In zebrafish, retinal damage induces the resident Müller glia to proliferate and produce neuronal progenitor cells that continue to amplify and migrate to the damaged retinal region, where they differentiate into the missing neuronal cell types. To develop neuronal regenerative therapies for humans, I am studying the mechanism of retinal regeneration in zebrafish. Previous studies demonstrated that Notch signaling inhibits retinal regeneration, and repressing Notch signaling is sufficient to induce Müller glial proliferation in the retina. The Notch receptor is processed through several cleavage events, one being facilitated by A Disintegrin And Metalloprotease 10 (ADAM10). ADAM10 has two paralogs in zebrafish, ADAM10a and ADAM10b. This project will study the role of ADAM10a and ADAM10b in zebrafish retinal regeneration. An ADAM10 inhibitor, GI2254023X, was injected intravitreally to selectively block activity of both ADAM10 paralogs. Tg(gfap:EGFP) transgenic fish were used to label Müller glial cells and Tg(Ath5:EGFP) transgenic fish were used to label Müller glial-derived neuronal progenitor cells. TUNEL expression confirmed that GI2254023X did not cause cell death in the injected eyes. However, GI2254023X-dependent ADAM10 inhibition was sufficient to induce Müller glial proliferation and produced neuronal progenitor cells in the absence of retinal damage. This demonstrates that ADAM10, like Notch signaling, is necessary to suppress Müller glial proliferation. To examine if ADAM10 acts through the Notch signaling pathway, I will be performing quantitative real-time PCR to examine the effect of ADAM10 inhibition on the expression of Notch target genes.

APC selectively mediates response to chemotherapeutic agents in breast cancer

Claire Bedalov
College of Science
Science Business
Katia Fernandez Soto
College of Science
Science Preprofessional Studies

Monica VanKlompenberg, Indiana University School of Medicine – South Bend Advisor: Jenifer Prosperi, Indiana University School of Medicine – South Bend, Harper Cancer Research Institute, and Dept. of Biological Sciences

The Adenomatous Polyposis Coli (APC) tumor suppressor is mutated or hypermethylated in up to 70% of sporadic breast cancers depending on subtype; however, the effects of APC mutation on tumorigenic properties in breast cancer remain unexplored. Using the ApcMin/+ mouse crossed to the Polyoma middle T antigen (PyMT) transgenic model, we identified enhanced breast tumorigenesis and alterations in genes critical in therapeutic resistance independent of Wnt/β-catenin signaling. Mechanistic studies in tumor-derived cell lines demonstrated that focal adhesion kinase (FAK)/Src/JNK signaling regulated enhanced proliferation downstream of Apc mutation. Despite this mechanistic information, the role of APC in mediating breast cancer chemotherapeutic resistance is currently unknown. We have examined the effect of Apc loss in MMTV-PyMT mouse breast cancer cells on gene expression changes of ATPbinding cassette transporters using real-time PCR. Additionally, we have utilized immunofluorescence to determine the proliferative and apoptotic responses of cells to chemotherapeutic agents cisplatin, doxorubicin and paclitaxel. We determined the added effect of Src or JNK inhibition by PP2 and SP600125, respectively, on chemotherapeutic response. We also used the Aldefluor assay to measure the population of tumor initiating cells. Lastly, we measured the apoptotic and proliferative response to APC knockdown in MDA-MB-157 human breast cancer cells after chemotherapeutic treatment. Cells obtained from MMTV-PyMT; ApcMin/+ tumors express increased MDR1 (multidrug resistance protein 1), which is augmented by treatment with paclitaxel or doxorubicin. MMTV-PyMT; ApcMin/+ cells are more resistant to cisplatin and doxorubicin-induced apoptosis, and show a larger population of ALDH positive cells. In the human metaplastic breast cancer cell line MDA-MB-157, APC knockdown led to paclitaxel and cisplatin resistance. In conclusion, both models showed that APC loss-of-function significantly increases resistance to cisplatin-mediated apoptosis. Furthermore, cisplatin in combination with PP2 or SP600125 could be clinically beneficial, as inhibition of Src or JNK in an APC-mutant breast cancer patient may alleviate the resistance induced by mutant APC.

Engineering T-cell receptors to optimize anti-tumor immunity

Orrin Belden
College of Science
Science Preprofessional Studies
Lance Hellman, Dept. of Chemistry and Biochemistry
Kelly Moxley, Dept. of Surgery, Oncology Institute, Cardinal Bernardin Cancer Center,
Loyola University Chicago
Advisor: Brian Baker, Dept. of Chemistry and Biochemistry

T-cells have demonstrated the ability to attack and kill various types of malignant cells in the human body. All nucleated cells in the body, aside from red blood cells, present antigens on their surface in complex with major histocompatibility complex (MHC) class I proteins. Recognition of malignantly transformed cells by T-cells is mediated through the T-cell receptor (TCR) interacting with the antigens presented by the MHC. Melanoma is a malignancy that is known to be immunosensitive. The primary immune antigen on melanoma cells presented by the MHC is the MART-1 (AAGIGILTV) peptide, which is recognized by a subset of TCRs known as DMF4 and DMF5. Clinical trials involving adoptive cell therapy (ACT) of melanoma patients showed cancer regression of 13% and 30% for clonally expanded T-cells genetically engineered to express DMF4 and DMF5, respectively. Our work involves using structure-guided computational design to enhance the affinity of DMF5 towards the MART-1 peptide and assessing the biological ramifications of these engineered TCRs in cell culture models. Thus far, we have generated and tested three higher affinity mutants of DMF5, αD26Y, βL98W, and αD26Y/βL98W, in both protein binding and cell culture experiments.

Capillary electrophoresis coupled to electrospray ionization-mass spectrometry for metabolomic analysis of tissue extracts

Danielle Boley
College of Science
Biochemistry
Norman Dovichi, Scott Sarver, Jennifer Arceo, and Nicole Schiavone
Dept. of Chemistry and Biochemistry
Advisor: Norman Dovichi, Dept. of Chemistry and Biochemistry

The proteome is commonly studied to improve disease understanding, but there is a need for improved small molecule analyses. The metabolome is useful for understanding downstream effects of cellular pathways and for identifying potential biomarkers. We aim to perform metabolomic analyses with capillary electrophoresis coupled to mass spectrometry (CE-MS). CE-MS is able to separate and detect a wide variety of metabolites while offering advantages in speed, efficiency, and limited sample consumption. Our preliminary results indicate differences in the types and amounts of metabolites present in healthy and sick mouse tissue extracts. Future work will include imaging MS to generate ion maps as a complement to CE-MS. Imaging MS provides us with locations of analytes within the tissue specimen. We will also run samples in positive and negative ion modes to identify metabolites that ionize preferentially.

Detection of Saimiriine Herpesvirus-1 in Saliva, Serum, and Tissue of Captive Bolivian Squirrel Monkeys

Carter Boyd
College of Science
Biological Sciences and Spanish
Advisor: John Vanchiere, Dept. of Pediatrics, Health Sciences Center Shreveport,
Louisiana State University

Human herpesviruses have long been studied for their importance in human health and disease. In comparison, there has been significantly less research on Squirrel Monkey herpesviruses, specifically Saimirine Herpesviruse-1 (SaHV-1). With increased human exposure to these animals in zoos, in animal research facilities, and homes as pets, understanding the viruses present in Squirrel Monkeys is important for considering possible zoonotic risk to individuals caring for these animals. This study sought to develop both conventional PCR and Real-Time PCR assays for SaHV-1, so that the virus can be detected and further studied in animal specimens supplementing the research data on the prevalence of these viruses. This information will be help to build more knowledge and understanding of these viruses for their research applications and potential risks to humans.

Make no bones without it: Induced mineralization of basicranial osteoblasts under 3D chondrogenic conditions

Justin Brill
College of Science
Biological Sciences
Holly Weiss, Dept. of Biological Sciences
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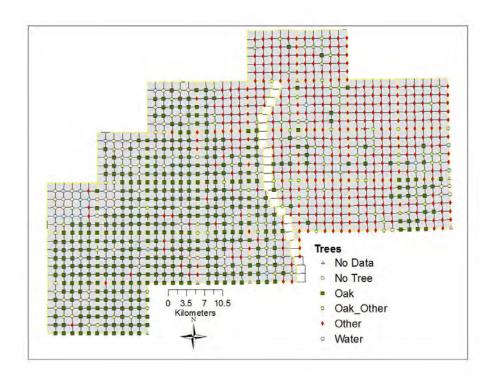
Osteoblasts (OBs) from the mammalian skull have traditionally been cultured in monolayer using an osteogenic culture medium to promote cellular differentiation and mineralization. However, after isolating and culturing basicranial OBs via standard methods, our initial experiments documented little mineralization. Therefore, we explored a novel induction method detailed below. Basicranial OBs from perinatal mice were isolated via outgrowth and plated as 100,000 cell micromasses. As micromass cultures, often referred to as multicellular aggregates, are known to better replicate in vivo conditions by mimicking 3D tissue structure, this procedure was used in conjunction with chondrogenic medium to induce mineralization. PrestoBlue assay was performed weekly to track cellular metabolic activity. Safranin O staining was performed after two weeks to evaluate cartilage deposition. To evaluate the extent of osteogenic differentiation, an Alkaline Phosphatase stain was performed after three weeks. Mineralization was directly observed after the fourth week via Alizarin Red staining. PrestoBlue analysis of the micromasses found that as time in culture progressed, there was a general decrease of metabolic activity, dropping sharply after the first week of culture. This potentially mirrors an endochondral mechanism where apoptosis coincides with matrix mineralization, causing drastic decreases in metabolic activity. Safranin O was observed to bind to very small portions of the stained micromasses, demonstrating that chondrogenic treatment did not induce purely chondrogenic differentiation. The ALP stain bound to several sites throughout the micromass cultures following three weeks, indicative of osteogenic activity. Alizarin staining identified considerable amounts of calcium deposited by the OBs, binding throughout most of each micromass. In sum, the application of chondrogenic medium to basicranial OB micromasses was shown to induce pervasive mineralization. However, the exact mechanism for this process requires further investigation. To this end, variability in micromass formation will be controlled so as to produce more uniform future results regarding OB activity.

Reconstructing the Pre-Settlement Forest of the Yellow River Watershed

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Jody Peters and Tamatha Patterson, Dept. of Biological Sciences Advisor: Jason McLachlan, Dept. of Biological Sciences

The Kankakee River watershed comprises over 5,000 square miles of northern Indiana and Illinois and, though having once been one of the largest wetlands in North America, has undergone human modification leading to increased sediment loads and overall ecosystem instability. The Yellow River, a tributary to the Kankakee in Indiana's Starke and Marshall counties draining 500 square miles, faces analogous erosion and soil deposition issues. Both watersheds lie in what was formerly a unique position: the boundary of the prairie peninsula and the deciduous forest biome of the eastern United States, Using tree composition data from the Public Land Surveys conducted in the 1820s and 1830s, this study aims to reconstruct the original forest pattern of the Yellow River watershed and find correlations with elevation, soil, and climate attributes to identify the major hydrologic determinants of the watershed before human modification. Tree species, diameter and distance from posts set every mile were used from thirty Indiana townships, for a total of 1055 data points. Species data were grouped as follows and localized to an ArcGIS map to visualize tree composition: Oak (only oaks present, n=434); Oak-Other (oak plus other tree species, n=114); and Other (only non-oak trees, n=405). East of the north/south line of the Michigan Road lands other non-oak species predominated while west of this boundary was primarily oak timber, a transition found to correspond with a decrease in elevation. Oak trees in the west were significantly larger and farther from the survey posts compared to non-oak trees in the east (average diameter Oak 42.4 cm, Other trees 36.8 cm, p<0.01; average distance 39.4 m, Other trees 14.5 m, p<0.01).



Modeling linear relationships between Indiana soil composition and tree data

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Climatic and physical environmental variables have been hypothesized to affect whether a prairie or forest dominates a particular area. With decreasing amounts of precipitation, the ability of soil to retain moisture is likely to play an important role in water uptake by plants, which could affect species composition and growth. Differences in soil composition may also lead to differences in vegetation biomass between soil types, as well as the CO2 sensitivity of the species living on various soil types. We compiled data from 19th century land survey notes (PLS notes) kept by the US government to obtain information regarding tree species composition, tree diameter, and estimates of tree abundance in the state of Indiana at the time of European settlement. Indiana is an important area of study because the Prairie Peninsula that extends throughout much of the Midwestern United States was thought to transition within Indiana to the Eastern United States forest structure. We created linear models to predict how changes in soil composition (percentages of sand, silt and clay) are associated with changes in tree species abundance, abundance of trees, and tree diameter along the Prairie Peninsula-Eastern Forest transitional areas. Data suggests that soil sand percentage has a significant positive relationship (p<0.05) with the distance between trees, while both soil silt and clay percentages have significant negative relationships (p<0.05; and p<0.05, respectively) with the distance between trees. This is consistent with our hypothesis that dense forest growth occurs in locations with greater soil water-retention capabilities, a property which is in part related to soil particle size.

Oral Presentation

Analysis of the Newell-Whitehead Equation

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Advisor: Xiaodong Cao, Cornell University

Differential Harnack estimates are a useful tool in the study of geometric flows on smooth manifolds. For example, in Perelman's celebrated proof of the Poincare conjecture, a differential Harnack estimate on the Ricci flow is one of many crucial steps. These estimates are still important today in geometric analysis, and can be employed in the analysis of general parabolic equations. We'll discuss this general approach and usefulness of these estimates, and then show how we can apply it to the Newell-Whitehead equation, a partial differential equation that describes certain phenomena in physics and materials science. After successfully obtaining the estimate, we'll discuss applications and conjectures we can prove using it.

Oral Presentation

A DFT investigation of the anions and neutrals resulting from dissociative electron attachment to thymine

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High energy radiation is known to cause cancer through inducing DNA damage. One of the major mechanisms through which it does so is dissociative electron attachment (DEA), where low energy electrons attach to molecules, cause the production of a high-energy transient negative ion (TNI), and then cause the breakdown of the molecule. In the present work, calculations were conducted to determine the optimized geometry and harmonic frequencies for each of the anion conformers that could result from DEA to thymine, one of the four major nucleobases in DNA. For all of the neutrals potentially produced from the process, the same information was calculated. The anion and neutral information allowed reaction enthalpies to be calculated for each known fragment mass. We deemed the reaction for a particular fragment whose enthalpy was lowest was identified as that fragment's most probable dissociation pathway. This study specifically increases our understanding of the process by which thymine is damaged by radiation, which more broadly augments our understanding of how radiation damages DNA.

¹Denifl, S.; Ptasinska, S.; Probst, M.; Hrusak, J.; Scheier, P.; Mark, T. D. Electron attachment to the gasphase DNA bases cytosine and thymine. Journal of Physical Chemistry A, 108, 6562-6569.

iLocater: A NIR Doppler Spectrometer

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iLoctater is a diffraction limited spectrometer that works in near-infrared wavelengths to detect earth-like exoplanets orbiting around M-dwarf stars, iLocater may be viewed as a follow-up to NASA's Kepler probe mission, by which NASA was able to confirm 246 exoplanets out of a pool of 3,601 planet candidates. It can also be used as a follow-up instrument for the upcoming TESS (Transiting Exoplanet Survey Satellite) mission. Both Kepler and TESS use the transit method to detect exoplanets, which involves analyzing light curves, and recognizing dips in intensity that correspond to planetary orbits. iLocater uses the radial velocity technique, which allows follow-up on much smaller planetary targets. With the transit method, the planet/star size ratio must be big enough that the intensity decrease is detectable by a satellite. With the radial velocity technique, where planets are detected by studying periodic motion in a star's radial velocity curve, smaller targets are more viable. Instead of looking for huge planets blocking light from huge stars, iLocater is looking for Earth-like planets that have a noticeable gravitational effect on small M-dwarf stars. Nonetheless, as the sizes of the objects decrease, the precision needed to measure these object increases. As a result, iLocater needs a fairly robust software suite to analyze the stellar data with the requisite precision. An integral part of our research focused on barycentric radial velocity correction, which involves correcting the star's radial velocity data for the Earth's motion around the sun. To observe a small star, wobbling about as fast as a quick shuffle, we had to correct for the Earth's motion to within mm/s, which had never been done reliably to this point. Additionally, we need to be able to read the data from our detectors which requires software to detect our spectral orders.

Unlocking global climate adaptation solutions: country resilience index to inform decision-making

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More intense and frequent natural disasters such as floods, fires, super-storms, and droughts brought about by climate change disproportionately affect the world's poor and vulnerable. The Dame Global Adaptation Index seeks to enhance the world's understanding of the importance of adaptation and facilitate public and private investments in vulnerable communities to improve livelihoods and save lives. To inform government, corporate, and development decision-making in adaptation, ND-GAIN measures country vulnerability and uniquely, readiness to accept adaptation investment.

Several insights about global adaptation needs and opportunities are visible in ND-GAIN. For example, the Index suggests that Scandinavian countries are among the most prepared for climate change, but that people living in the least developed countries face 10 times more chance of being impacted by a climate disaster. The poorest countries will take over a century to reach the same level of resiliency of the wealthiest ones. Despite this, some of the most vulnerable countries like Rwanda have made great strides in readiness in the past 5 years, indicating the time is ripe for adaption investment.

ND-GAIN engages adaptation thought leaders at its Annual Meeting and corporations through its Corporate Adaptation Prize. In 2014, over 20 companies submitted projects, judged for their measurable adaptation impact, scalability, and market impact. The Centre de Suivi Ecologique (CSE) and Novartis International AG were identified as adaptation leaders for their work on combating coastal erosion in Senegal to protect local fisheries and tourism, and for the Healthy Family initiative that merges social and business models in sustainability, respectively.

ND-GAIN is currently developing several key features of the organization and the Index to increase its engagement with stakeholders and global leaders. For example, it leads a project using five US pilot cities to develop an Urban Adaptation Assessment framework, seeks to better understand corporate adaptation practices and needs, and reaches out to world leaders at major climate talks.

Implications of salmon-derived nutrients in non-native streams: Investigating the influence of salmon-derived Ca and P in Hunt Creek, Michigan

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Pacific salmon (*Oncorhynchus* spp.) release nutrients into streams when they return to spawn and die. Studies in native salmon streams suggest salmon-derived nitrogen (N) and phosphorus (P) can alleviate limitations on biofilm growth, both individually and as co-limiting nutrients. However, such alleviation has been poorly studied where salmon have been introduced, especially regarding less considered nutrients such as calcium (Ca). Calcium is biologically important given its buffering capacity and role in physiology and development. Our objective was to determine biofilm response to modification of stream nutrient availability by the presence of non-native salmon spawners in Great Lakes tributaries. Furthermore, we focused on the interaction between Ca with P, which has been shown to affect the bioavailability and uptake of both elements. Nutrient limitation was assessed using nutrient-diffusing substrates (NDS) infused with Ca, P, or Ca+P, and deployed in separate reaches of Hunt Creek, Michigan, where salmon carcasses were added (downstream, treated) or were absent (upstream, control), both before and after the addition. Biofilm growth was determined from levels of chlorophyll a in biofilm that accumulated on each NDS. We predicted that Ca and P would be individually limiting or co-limiting in both reaches without carcasses, and such limitation would be alleviated downstream with the carcass addition. Multiway ANOVA statistical analysis provided little evidence of Ca and P limitation. However, P had a slight inhibitory effect on biofilm growth. Lack of nutrient limitation suggests that carcasses of introduced salmon are unlikely to increase stream productivity indirectly through biofilm nutrient uptake. Our results, supported by observations from a larger study involving this carcass addition, suggest biofilm growth is limited largely by seasonal changes in light and background nutrient concentrations. Overall, our study emphasizes the important of these local environmental factors in the influence of salmonderived nutrients.

Effect of Spatial Repellents on Dengue Vector Attractancy Behavior

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The Aedes aegypti mosquito is considered to be the principal vector of Dengue virus (DENV) that causes dengue fever, an arthropod-borne disease of global burden with incidence growing to estimates of approximately 50-100 million infections worldwide annually. Although efforts are underway for development of a DENV vaccine, recent evidence indicates that a single tool will not be effective for control of dengue fever. Prevention relies primarily on vector control through use of indoor application of residual insecticides, specifically in the pyrethroid chemical class. However, the efficacy of such strategies is threatened by increasing levels of pyrethroid resistance. Alternatively, pyrethroids that are characterized as spatial repellents – those that are highly volatile at ambient temperatures – have received new interest as insecticide resistance mitigation tools since they function to reduce biting through behavioral changes in mosquitoes versus directly killing them. A rigorous understanding of the behavioral effects these volatile pyrethroids have on mosquitoes is critical to understanding the overall impact on survival and reproduction of vector populations and therefore expectations of protective efficacy against pathogen transmission. We predict that exposure to volatile pyrethroids will decrease attraction of mosquito vectors to experimental oviposition sites. To test this hypothesis, gravid (egg-laying) Ae. aegypti have been used to optimize an oviposition attractancy bioassay and confirm a spatial repellent response to target spatial repellent chemicals and measure change in attractancy between repellentexposed and non-exposed test populations. Findings from this study can be used to facilitate how these volatile pyrethroid chemicals are used in the field. A significant decrease in attractancy of egg-laying Ae. aegypti mosquitoes to potential breeding sites post-repellent exposure would indicate that there is considerable viability in using spatial repellents to decrease the overall vector population thereby reducing the probability of human-mosquito contact and DENV transmission overtime.

Synthetic Routes to New Redox-Active Ligands

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In contrast to traditional oxidation reactions, where metal centers gain or lose electrons, so-called "nonclassical" mechanisms, where the redox changes take place on the ligands, are attracting significant interest. Developing new ligands for these reactions is thus important. A palladium complex containing simple, unlinked amidophenolate ligands has been described as a neutral, diamagnetic, square planar complex containing two bidentate O,N- coordinated radical ligands. Initial attempts to synthesize a bis(aminophenol) ligand with a 2,3-dimethyl-2,3-butanediyl linker proved unsuccessful. Further attempts to create such a ligand included directed C-H activation on model substrates made by reacting various phenols with several isocyanates. Preliminary results using this retrosynthetic strategy have not yet resulted in the formation of the ligand. In the absence of chelating tetradentate ligands, the reactivity of the palladium bis(iminosemiquinonate) complex is being explored.

With the appropriate ligand, it will be possible to characterize the relevant palladium compound and test its ability to oxidize substrates. Comparison with the reactions of similar known compounds that cannot accommodate both hydrogens on the same face of the compound should indicate whether the reaction is stepwise or concerted. This research could lead to the discovery of a novel oxidation mechanism. This has importance in designing new catalysts for useful transformations, especially in the selective reduction of CO2.

Oral Presentation

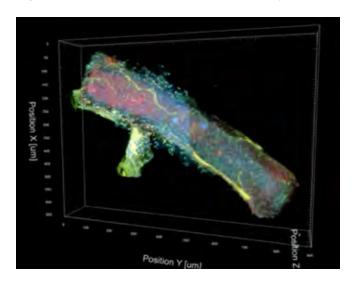
Reveal3DTM: A Microfluidics Platform for Enabling High-Throughput Characterization of Breast Tumors and the 3D Microenvironment In Situ

Kyle Cowdrick College of Engineering Chemical Engineering

Cody Narciso and Teresa Brito-Robinson, Dept. of Chemical and Biomolecular Engineering Advisors: Siyuan Zhang, Dept. of Biological Sciences, David Hoelzle, Dept. of Aerospace and Mechanical Engineering, and Jeremiah Zartman, Dept. of Chemical and Biomolecular Engineering

Approximately 90% of all cancer fatalities are due to metastasis—the spreading of primary tumor cells to distant organs. While our understanding of the crosstalk between tumor cells and various molecular, cellular components of the metastatic microenvironment plays a critical role in dictating the outcome of metastatic breast cancers, the translation of preclinical research from the bench to the bedside is intrinsically challenging owing to the unique spatial and temporal nature of tumor-tumor microenvironment (TME) interactions. Traditional immunohistochemistry (IHC) based biopsies continue to serve as the gold-standard for cancer diagnostics. However, this standard remains limited owing to the inability of thin tissue slices to faithfully interrogate the TME. As such, there is an urgent clinical need to develop a robust platform that can systematically integrate genetic and morphological information from precious patient biopsies and provide faster, more accurate diagnoses of early stage metastases.

This daunting clinical challenge is addressed with Reveal3DTM. Reveal3DTM is a novel, automated, IHC-based diagnostic platform capable of handling 3D patient biopsy samples. This prototype combines cutting-edge tissue clearing, multiplexed IHC labeling, and whole-mount imaging with high-throughput microfluidic device design. Microfluidics offers an ideal solution to the problems faced by cancer diagnosticians by combining micron-sized channels with complex fluid-handling operations to reduce reagent consumption and automate the diagnostic procedure. Automation of diagnostic process will overcome limitations in clinical cancer diagnosis by ensuring greater diagnostic reproducibility and increasing the throughput of tumor biopsy analysis. Reveal3DTM will equip the diagnostician with unprecedented information about the precise nature of the patient-specific cancer being treated. Reveal3DTM is poised to significantly enhance a physician's ability to perform "precision oncology" by providing comprehensive analysis of metastatic tumors and tumor microenvironments. These advancements will improve the accuracy of clinical prognosis, mediating the success of anti-cancer therapeutics by overcoming the current limitations in IHC-based assays.



Screen to identify Mycobacterium marinum strains that are non-cytotoxic to amoeba

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Tuberculosis (TB) is the second largest killer after HIV/AIDs among single infectious agents. Multi-drug resistant TB is observed worldwide (WHO, 2014). The current vaccine for TB, the BCG vaccine, is not fully preventative and is not used in the US (CDC, 2014). To build a better vaccine, we need to expand our understanding of how the causative agent of TB, Mycobacterium tuberculosis, interacts with its host. M. tuberculosis requires an intact ESX-1 secretion system for virulence. The mechanism of how ESX-1 mediates virulence is unclear. We propose to identify novel genes required for ESX-1 secretion to better understand it. Our study used Mycobacterium marinum, an established model organism in which ESX-1 secretion is conserved and necessary for cytotoxicity to Acanthamoeba castellanii, a free-living phagocyte. To find unknown ESX-1 genetic components, we performed a screen on a transposon insertion library of M. marinum strains by testing their ability to lyse A. castellanii. We infected A. castellanii in 96 well plates with M. marinum strains at unknown multiplicity of infection (MOI). We then selected non-cytotoxic strains using optic microscopy. Non-cytotoxic strains underwent a second round of screening at an MOI of 10, with two replicates. Strains that were non-cytotoxic in the second round of screening were further characterized by red blood cell lysis assay. Twelve plates or ~1000 strains were screened, and seven mutant strains were identified. These strains failed to lyse red blood cells, a mycobacterial phenotype that requires a functional ESX-1 system. Further characterization of the ESX-1 phenotypes as well as genetic mapping to determine the gene responsible for the phenotype are underway. Our study provides a screening method for ESX-1 deficient mycobacterial strains. These strains will be further studied to identify genetic components of ESX-1 secretion, enhancing our understanding of mycobacterial infection so it can be targeted and prevented.

Creating Environmental Policy for the Great Salt Lake: Effects of ammonia, copper, and lead on brine shrimp (Artemia franciscana) mortality from the Great Salt Lake, Utah, U.S.

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As human civilization advances, human society is increasingly impacting the natural environment causing the problem of ecosystem degradation to grow. Because of this escalating anthropogenic burden on natural ecosystems, this study examines how expanding human industry is affecting brine shrimp (Artemia franciscana) populations in the Great Salt Lake (GSL), Utah. Ecotoxicology assays were conducted to examine the effects of ammonia, copper, and lead on brine shrimp mortality, pollutants listed as priority pollutants by the Environmental Protection Agency. Although exact sources of these pollutants are unknown, it is believed that waste from industrial mines and metal smelters and runoff from urban and agricultural areas are the prime origins. Based on recent water quality assessments, average dissolved levels of ammonia, copper, and lead are estimated as 380 μ g/L, $4.2 \pm 2.1 \mu$ g/L, and 2.04 ± 0.34 µg/L, respectively. Acute assays for ammonia and copper were conducted in order to determine the concentration producing 50% mortality (LC50), and the lowest concentration producing a significant increase in mortality (LOEC). Acute assays using lead were completed over a range of salinities and lead concentrations due to low solubility of lead in brine. Trials lasted 96 hours and each replicate contained 20 brine shrimp nauplii. Each replicate was counted for surviving nauplii every 24 hours and brine was also replaced on a static-renewal basis every 24 hours. Based on survival analysis, the LOEC for ammonia was 2,706,315.08 μg/L and the LC50 was 3,005,920.08 μg/L. For copper, the LOEC was $118.16 \mu g/L$ and the LC50 was $161.75 \mu g/L$. Although these values are well above current average GSL estimates of these toxins, these data suggest that copper is roughly 18,583 times more toxic to brine than ammonia, and inputs of copper should be strictly monitored. With respect to lead assays, brine shrimp mortality was significantly higher in low-salinity/high-lead replicates, suggesting that lower brine salinities allowed more lead to dissolve into solution. These data imply that brine shrimp susceptibility to lead increases in lower salinities however further tests on lead are necessary before a decision can be made on proper lead regulation strategies.

Outdoor Insecticide-Impregnated Barriers: A New Intervention for Malaria Control in the Solomon Islands

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Malaria is a mosquito-borne disease that affects millions of people each year, with over 600,000 deaths globally in 2012. Recently, Solomon Islands set a goal of nationwide malaria elimination. Decades of long-lasting insecticidal nets (LLIN) and indoor residual spraying (IRS) interventions have greatly reduced, but not eliminated malaria in Solomon Islands. Instead, the primary malaria vector, Anopheles farauti, has undergone a shift from late-night endophagic bloodfeeding to early-evening exophagic bloodfeeding. Presumably, these behaviors are selected for by LLINs and IRS, which may have reached the limit of their effectiveness. Thus, behavioral resistance could be a contributing factor to the persistence of malaria transmission. Our project is testing the effectiveness of a novel outdoor intervention called insecticide-impregnated barriers (IIBs) at reducing malaria transmission in Western Province, Solomon Islands. In summer 2014, we mapped study villages using geographic information system (GIS) devices, constructed IIBs in intervention villages, and distributed radical cure treatment to members of our incidence-monitoring cohorts. The incidence of malaria infection in the cohorts will be monitored over the next 2 years and compared between IIB villages and control villages. Mosquitoes are also being collected in human landing catches to determine species composition, infection rates, and changes in age structure over the ensuing study period. We hypothesize that the IIBs will reduce malaria transmission over the study period as a result of the strategic placement of the interventions. Early results show low, but persistent malaria transmission in Western Province. Four species of human Plasmodium, and an abundance of human-biting Anophelines were found.

Oral Presentation

The Evolution of Sexual Isolation in the Seed Beetle, Callosobruchus maculatus (Coleoptera: Chrysomelidae)

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Frank Messina, Dept. of Biology, Utah State University Advisor: Jeffrey Feder, Dept. of Biological Sciences

Ecological speciation is a process by which barriers to gene flow evolve between populations due to ecological divergent selection between environments. One specific type of isolating barrier, sexual isolation, reduces the rate of copulation between diverging populations during secondary contact. In many taxa, the evolution of sexual selection is rapid. However, without knowing when diverged lineages initially split, knowing how rapid is difficult. Examples of sexual isolation are prominent among plant-feeding insect specialists. To better understand the rate and pace of the evolution of sexual isolation we conducted experiments using the seed beetle, *Callosobruchus maculatus* (Coleoptera: Chrysomelidae), a specialist of dried legumes. We have artificially induced a host shift from the ancestral mung to three separate lentil populations that were then reared for approximately 100 generations. We performed crosses between each line and itself as a control, each lentil line with the ancestral mung line to measure degree of sexual isolation, and each lentil line with the other lentil lines to determine the potentially different developmental rates of sexual isolation. We measured a suite of response variables including (1) presence of copulation, (2) time to copulation, (3) time spent copulating, (4) length of the first copulation and (5) length of the longest copulation. Initial results suggest that sexual isolation may be evolving between host-associated *C. maculatus* lines, and that it may be evolving convergently.

Community Composition of the Burgess and Chengjiang Shales (Drumian and Atdabanian ages of the Cambrian Period)

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The Cambrian period was a watershed age of the history of life on Earth, when life underwent a major paradigm shift from mainly unicellular, simple organisms to complex, multicellular ones. This rapid diversification, called the Cambrian explosion, lead to the evolution of all animal phyla living today. Two major fossil formations showcase this rapid change in biota: The Chengjiang beds dating back to about 515 million years ago, and the later Burgess Shale from 508 million years ago. The Museum of Biodiversity has a collection of 261 specimens from these two formations, with 52 from the Chengjiang beds and 209 from the Burgess Shale. Of these, 182 specimens were identified and classified based on current cladistic analyses and online databases, 23 from the Chengjiang beds and 159 from the Burgess Shale. These fossils were photographed and catalogued. The vast majority of specimens were Arthropods, with the second largest group belonging to Brachiopods. However, the specimens were diverse as well as concentrated, with fossils coming from chordates, mollusks, sponges, and even plants and bacteria. Among the arthropods, trilobites made up the largest group, with genera such as *Elrathia*, *Elrathia*, Kootenia, Ogygopsis, and Olenoides heavily represented. The most common brachiopod present was Paterina zenobia. Some of the rarer genera included the sponge Vauxia, the chordate Pikaia, the arthropods Anomalocaris and Marella, the bacterium Marpolia, and the plant Dictyophycus. This wide diversity and abundance of organisms highlights the dramatic change in life during the Cambrian period.

Design of Micro-Pattern Gas Detectors

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In the field of nuclear physics, the development of methods to precisely determine key parameters in nuclear reactions is an important area of research. One of the methods recently developed is the active-target method where charged-particle tracks inside of a gas volume are imaged. The images are created from the measurement of electrons originating from the ionization of the gas by the traversing charged particles. These electrons are amplified and detected by what are called Micro-Pattern Gas Detectors. We are currently developing the electrode pattern of Micro-Pattern Gas Detectors using the Printed Circuit Board design software, Altium Designer. While various designs of electrode patterns already exist, our plan is to create one that would allow us to more easily image reactions that produce multiple charged-particle tracks. This new design will increase the number of anode electrodes and cover the entire plane of the detector. This will allow us to more precisely image tracks of charged particles involved in nuclear experiments planned at the Nuclear Science Lab at Notre Dame.

Oral Presentation

Investigating Nephrogenesis through Chemical Genetics: Insights into Peroxisome Proliferator-Activated Receptor (PPAR) Signaling during Zebrafish Kidney Development

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Chemical genetic screening is the phenotypic assessment of small molecules to determine if they can alter signaling pathways and other biological processes in vivo. Zebrafish are a useful model for chemical genetic investigation due to their strong genetic conservation with humans and their ability to absorb small molecules through their chorions during early development. Retinoic acid (RA) signaling is essential for establishing discrete proximo-distal nephron cell lineages, and treatment with exogenous RA, RA synthesis inhibitors, and/or retinoic acid receptor alpha (RARα) coregulators disrupts these fates. Further analysis has not been conducted, hence we began a chemical genetic screen of the ICCB Known Bioactives Library to gain novel insights into how small molecules affect nephrogenesis. We found that 78/480 compounds induced relevant morphological defects, including compounds that regulate peroxisome proliferator-activated receptor (PPAR) activity. This indicates a previously uncharacterized role for PPARs in nephrogenesis. In-depth characterization showed that PPAR agonist bezafibrate promotes proximal segment identities at the expense of distal segments analogously to exogenous RA treatments. Conversely, PPARy antagonist GW-9662 expanded distal regions at the expense of proximal regions. The bezafibrate-induced phenotype parallels phenotypes induced by prostaglandins also discovered during the screen, suggesting a relationship between the two pathways. Finally, preliminary morpholino knockdown of PPARγ coactivator 1-alpha (PGC-1α) showed a combination of proximal and distal effects. Future studies will delineate when in development PPARs affect nephrogenesis, identify specific PPAR isoforms involved, and investigate the link between PPARs and prostaglandins, As PPAR coregulators are used clinically, understanding how they affect development is critical. This undertaking has given us not only new insights into nephrogenesis and segment boundary formation but also hope in the fight against renal progenitor mispatterning diseases. These novel findings can also be applied to stem cell research and tissue engineering, bringing us to the threshold of translational science.

Exercise During Treatment for Pediatric Oncology Patients: A Retrospective Survey

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Introduction: Exercise training during cancer treatment improves fatigue and other negative effects of treatment in adults. The aim of this retrospective survey was to compare exercise habits and Quality of Life (QOL) of a pediatric oncology population with a variety of cancer diagnoses.

Methods: Following IRB approval, an informational mailing was sent to 125 previous participants of Camp Mak-A-Dream (Missoula, Montana). An anonymous survey was sent to those who responded. All who were diagnosed with cancer prior to the age of 18 were eligible. The QOL survey was the FACT-G which consists of four parts: physical, emotional, social, and function well-being. Exercise levels (in hours/week) were determined using the National Cancer Institute's Familial Breast and Ovarian Cancer Study as a template. The values were scored and subtracted to give relative exercise levels (difference of hours exercised before and after diagnosis). The exercise and QOL scores were compared using the Pearson Product-Moment Correlation test.

Results: The respondent population was primarily in their teenage years, diagnosed Blood or Brain cancer, and the majority reported a physical limitation due to illness. Treatment length varied (with mostly 3-12 months or 1-2 years of treatment) and 40% of the participants had a cancer recurrence. The average exercise reported for the group before diagnosis was 110.4 minutes/week, while average after diagnosis was 32.1 minutes/week. The average relative exercise duration was 78.3 minutes/week with a standard deviation of 26.4 minutes/week. The mean QOL for the population was 44 (out of a possible 92). The QOL and relative exercise level values were then correlated for each participant, giving an R value of 0.3635. This indicates a positive, medium strength correlation.

Conclusions: This analysis suggests that exercise may influence QOL in a pediatric oncology population. Given the strong data demonstrating positive effects of exercise training in the adult oncology population, our analysis suggests that exercise may also be beneficial in the pediatric population.

Antioxidant enzyme-mediated survival of ECM-detached breast cancer cells requires AMPK activation

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Normal epithelial cells require attachment to the extracellular matrix (ECM) for proper maintenance of metabolic function and survival. However, it has recently become clear that cancer cells must alter their metabolism during times of ECM-detachment in a fashion that promotes their survival. We have discovered that breast cancer cells utilize the activity of antioxidant enzymes to eliminate the detachment-induced elevation in reactive oxygen species (ROS). This decrease in ROS relieves the inhibitory effects that ROS have on fatty acid oxidation (FAO) that in turn facilitates ATP production during times of energy deprivation. Interestingly, this critical role of antioxidant enzymes is not evident in ECM-attached cells suggesting that targeting antioxidant enzymes may be an effective strategy to eliminate ECM-detached cells. Furthermore, our studies have revealed that the molecular mechanisms controlling the regulation of FAO by antioxidant enzymes involve modulation of AMPK protein levels. Thus, our data reveal that antioxidant enzymes and AMPK signaling may be attractive targets for the design of novel therapeutics aimed at eliminating ECM-detached cancer cells.

A fast, recursive normalization algorithm for vignetting correction of large sample montages

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With the emergence of quantitative fluorescent microscopy in cancer biology research, high-resolution images of large tumors have become necessary to understand cell-level phenomenon contributing to tumor growth and metastasis. To generate these datasets, images from multiple stage positions are often acquired and then stitched together in the form of a mosaic that encompasses the entire specimen. Fluorescent micrographs naturally exhibit darkening around the edges, or vignetting, which makes seamless stitching challenging. When this artifact is not corrected, the stitched image will have visible seams where the individual images overlap, introducing a systematic error into quantitative analysis. Specifically, vignetting artifacts in confocal montages can be reduced through the use of low-frequency Fast Fourier Transform filtering followed by tile normalization. An algorithm was developed to recursively normalize tile intensities through global parameter optimization, and was shown to be more effective than alternative vignetting correction methods. The recursive nature of the normalization results in nearly linear scaling of computational time with size. Furthermore, unlike many other algorithms, this method has been found to work with objects of different scales, including nuclei, cell boundaries, and multi-cellular landmarks. This image-processing pipeline can be applied to high-resolution whole-tumor images to potentially improve the quantification of gene expression levels and segmentation accuracy, and will be available as an open-source, stand-alone program.

Localization of ZNF217 and PKM2 in Breast Cancer Cell Lines

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In the United States, breast cancer is the second leading cause of cancer deaths in women. While overall breast cancer patient mortality has declined, the mortality rates of patients diagnosed with the most advanced breast cancers have not changed largely because biomarker tools that predict patient outcomes and treatment response are lacking. A novel breast cancer biomarker and drug target is the oncogene ZNF217 that is overexpressed in approximately 25% of breast cancer patients. Overexpression of ZNF217 correlates with increased chemoresistance, increased metastasis, and reduced patient survival. To identify additional proteins that interact with ZNF217, our collaborator Dr. Colin Collins, Vancouver Prostate Centre, and his team used ZNF217 as bait in a two-hybrid screen and identified a panel of interacting proteins. They discovered that ZNF217 physically interacts with PKM2, an isoform of pyruvate kinase, the enzyme responsible for the conversion of PEP to pyruvate in the last step of glycolysis. An increase in PKM2 leads to high levels of lactate by increasing aerobic glycolysis ("Warburg effect") and allows cancer cells to flourish under oxygen deficient conditions. The focus of our study is to determine the cellular localization of the interaction between ZNF217 and PKM2 in order to uncover the significance of their interaction in breast cancer and to provide insights into the molecular mechanisms of how ZNF217 promotes poor patient prognosis. We find, in human breast tissue, ZNF217 is predominantly nuclear but can be cytoplasmic in some patient samples. PKM2 can also localize to the nucleus where it acts as a histone kinase and affects gene expression. We hypothesize that nuclear localized PKM2 is the isozyme to be interacting with ZNF217 and this interaction promotes breast cancer progression by regulating the gene expression of a pro-cancer gene expression pathway. We also observed a truncated form of ZNF217 localizing to the cytoplasm. This isoform could be interacting with PKM2 to alter metabolic pathways. The studies will be foundational for the development of biomarker assays that use ZNF217 as a novel biomarker and drug target for more personalized treatment options in breast cancer patients.

Modernizing Plunger Control with Low-Cost Digital Electronics

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The plunger technique provides a valuable tool for measuring lifetimes of excited states in the 1-100 ps range. The plunger consists of a thin foil target and stopper foil separated by some controllable distance; beam-induced reactions occur in the target and the resulting nucleus of interest leaves the target foil and is completely stopped by the stopper foil. The Doppler-shift in γ -ray energy due to the velocity of the deexciting recoiling nucleus is used to count the fraction of transitions that occur during the flight time, thus giving the mean lifetime of the gamma-ray depopulating a specific nuclear state directly. This technique, called the Recoil Distance Doppler-Shift (RDDS) method, requires precise and stable positioning of the foils over periods of hours or longer while correcting for beam-induced deformations to the foils. The Notre Dame Nuclear Science Laboratory has a plunger device that is approximately 30 years old. Our work included the upgrade and full rebuilding of the electronics to control the plunger system. In the Notre Dame plunger apparatus, the separation between foils is measured via capacitance between the foils and is used to control the position of three servo motors. We have made two major upgrades to the plunger device: (1) a newly-applied, precision capacitance-measuring circuit using an integrated circuit originally designed for touchscreen sensors, (2) and low-cost microcontroller-based feedback loop for precisely controlling servo motors with quadrature encoder outputs. The capacitance measurement follows the proliferation of touchscreens and touch sensors. The microcontrollers are also a significant modernization of the plunger. Once we have demonstrated that all the mechanical parts of the plunger work as desired, we will carry out reactions in the Nuclear Science Laboratory and will measure the lifetimes of excited states in several rare earth nuclei.

APC in Breast Cancer: the ABCs of gene expression

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Breast cancer is the most common malignancy and cancer-related cause of death in non-smoking women in the United States. Due to the heterogeneity of this disease, the oncogenic and signaling pathways contributing to these tumors are distinct. The Adenomatous Polyposis Coli (APC) tumor suppressor is mutated or hypermethylated in up to 70% of sporadic breast cancers; however, the mechanism by which APC mutation impacts tumorigenesis remains unexplored. Up-regulation of the zinc finger transcription factor EGR-1 has been associated with cell invasion and enhanced drug resistance, which is an important property of cancer stem cells (CSCs). ALDH1 and STAT3 have been useful in the identification of CSCs, which are associated with poor clinical outcomes including increased tumor survival and invasion. We utilized two human breast cancer cell lines, MDA-MB-157 and DU4475, and cells isolated from the Mouse Mammary Tumor Virus-Polyoma middle T (MMTV-PyMT); ApcMin/+ mouse model. APC was knocked down in the MDA-MB-157 cells through shRNA lentiviral transduction, or transfected into DU4475 cells. First we looked at the expression of the transcription factor EGR-1 through Real-Time PCR in the MDA-MB-157 and DU4475 cell lines. Next, ALDH1 and STAT3 were measured in the MMTV-PyMT;ApcMin/+ mouse model and in MDA-MB-157 cells through western blots. In addition, an ALDEFLUOR assay was used to measure ALDH1 activity in the mouse model. EGR-1 expression was increased in both MDA-MB-157 APC-knockdown and DU4475 APC-mutant cells compared to cells expressing APC. In addition, STAT3 expression was found to be increased in MDA-MB-157 APCknockdown and MMTV-PyMT; ApcMin/+ cells compared to MDA-MB-157 APC-wildtype and MMTV-PvMT:Apc+/+ cells. ALDH1 activity and tumor development were enhanced in ApcMin/+ cells compared to control cells. Combined, these data suggest that APC knockdown increases tumorigenic properties of cancer cells through EGR-1 overexpression and modulation of known cancer stem cell markers, ALDH1 and STAT3. Future studies will include measuring the expression of EGR-1 in the MMTV-PyMT; ApcMin/+ cells as well as ALDH1 in the human cell lines. Furthermore, because of the overexpression of these genes and markers, strategies designed to target positive populations might lead to more effective therapies of APC-mutant breast cancers.

Characterization of Neuropeptide Y Receptor in Aedes aegypti Mosquitoes through RNA Interference

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Aedes aegypti mosquitoes are the principal vector for dengue fever in addition to the vector for chikungunya and yellow fever. Collectively these diseases affect over one million people each year, predominantly women and children in Sub-Saharan Africa. Vector control via insecticide development is therefore a crucial component of global health initiatives to decrease disease burden in the Global South. G Protein Coupled Receptors (GPCRs) are an important target for insecticide development as these cell-surface receptors are involved in a variety of important biological pathways. This research examines the expression and function of the Neuropeptide F Receptor (NPF) in A. aegypti mosquitoes through RNA interference with double-stranded RNA (dsRNA). NPF which is the homolog of Neuropeptide Y in vertebrates has been shown to be important for many physiological processes including socialization, foraging, and feeding which make it a key target for insecticide development. dsRNA was synthesized for both the A.aegypti NPF receptor and its ligand. Knock-down was observed using Real-Time Quantitative PCR. The effect on mosquito phenotype as a result of the knock-down was examined through sugar feeding and blood feeding assays to determine whether or not decreased NPF levels alter mosquito behavior. This study will help determine whether antagonizing the NPF receptor is a good target for commercial insecticide development.

Photic modulation of Anopheles gambiae mosquito behavior

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Biting behaviors in anopheline mosquitoes are time-of-day specific, with a greater abundance of biting occurring during the dark phase of their photoperiod (Rund et al., 2013, Scientific Reports 3: 2494). We investigated whether a single light pulse administered during the early dark phase of the LD cycle would inhibit biting behavior. An. gambiae locomotion/flight activity has a distinct circadian rhythm, characterized by nocturnal activity. We investigated how precise light pulses delivered throughout the circadian cycle can shift the flight activity rhythm, leading to the synthesis of an An. gambiae Phase Response Curve (PRC). Mosquitoes were maintained on a 12:12 LD cycle, including 1 hr dawn/dusk simulations. To investigate biting, two An. gambiae strains (S and M molecular forms) were treated with white light (10 min, 150-800 lux) at the onset of dark phase of the LD cycle (ZT12; end of dusk), and the percentage taking a blood meal was recorded. To produce an anchored PRC, S-form mosquitoes received a single 30 min pulse of light (300 lux) at various times during the immediate 24 hr transitioning from LD to DD. The pulse significantly reduced biting tendency in the S-form for 2 hr after administration (at 0.20 hr and 2 hr), with variable responses observed at 4 hr, and no differences detected at 6 and 8 hr (one factor ANOVA, p<0.05). Conversely, M-form mosquitoes were unresponsive to the light treatment, i.e. their biting tendency remained high (n.s.). For the PRC analysis, An. gambiae mosquitoes demonstrated distinct delays and advances in circadian phase when light was presented during the early and late subjective night, respectively. These data reveal a strain-specific effect of light on biting behavior that is both immediate and sustained. At present, insecticidal treated bed-nets designed to prevent mosquitohuman contact are heavily relied upon to prevent malaria transmission; as mosquitoes and malaria parasites are becoming increasingly resistant to insecticidal and drug treatments, there is a necessity for the ongoing development of novel and innovative control strategies. The inhibitory and phase shifting effects of light may prove to be an effective tool in assisting with these strategies.

Hemispheric Equalization of Auditory Responses in Pediatric Single-Sided Deafness

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Among children with single-sided deafness (SSD), some have no difficulties with everyday listening environments (e.g., hearing in noise), while other children have difficulties, putting them at a disadvantage in academic and social settings. These high- and low-performing children are medically identical, making early intervention in the low performing cases difficult. Normal-hearing (NH) adults with SSD typically have adapted to unilateral hearing loss by exhibiting "equalized" bilateral hemispheric responses to monaural stimuli. We hypothesize that NH children and high-performing children with SSD will display similarly "equalized" brain responses to monaural stimuli. To test this, we obtained EEG data from 12 pediatric subjects (SSD n=3, NH=9) in response to monaurally presented tone bursts, temporal changes, and spectral changes. Average waveforms and single-dipole source waveforms were obtained for each ear in response to each stimulus type. The resulting data suggest that usable EEG signals can be obtained from children with SSD, and that NH children and high-performing children with SSD display equalized hemispheric responses to monaural stimuli. The study was limited by the small sample size, but has demonstrated the feasibility of continuing the investigation on a larger scale.

Bridge Length vs Bridge Bend

Bridget Goodwine Christ The King School

Introduction - In this experiment I constructed a yardstick bridge to discover how the bridges bending increased in relation to the bridges length increasing. I found a formula to predict how much a bridge will bend under weight. Finding a formula like this would greatly aid bridge engineers in the design of their bridges, even though bridge designers have many obstacles to overcome. No matter what other effect (aside from the deduction of gravity), if there is too much weight on a bridge, it will collapse. This formula will help improve the safety of bridges.

Hypothesis - If the length of a beam or bridge is doubled, it will bend twice as much under the same amount of weight.

Procedures - Set up the wooden rises 12 in. (30.48 cm.) away from each other to use as supports for your bridge. Balance the yardstick on the two rises, forming a bridge. Record the length of the yardstick bridge Measure and record the distance between the ground and the top of the yardstick at the center between the supports (record the data under unbent). Place the tile (or other weight of about ?????) on the center of the yardstick, causing the yardstick bridge to bend under the weight. Measure and record the distance between the ground and the yardstick at the center between the supports (record the data under bent). Find the total length that the bridge bent by subtracting the unbent measurement from the bent measurement (record the data under total bend). Repeat steps 2.-6., changing the length of the bridge (by changing the length of the rises the vardstick rests on) to 16 in., 20 in., 24 in., 28 in., and 32 in. Perform three trials of steps 1-7. Find the average (add the results of the total bend together and divide the result by the number of numbers you added up) of the total bend of the three trials for each length. The set up for the formula that can be discovered for finding the total bend is bend (b) = a (coefficient) times length (length of the bridge) raised to some power: b=aLp, where b is the amount of bending, a is a coefficient we have to determine, L is the length of the bridge and p is a power we have to determine. Looking at the plot of the bending, guess the power. Then change the coefficient so that the largest bending point matches. Graph the average total bends and the total bend of your formula to discover if you need to change your formula. Change your formula until the formula and the average total bend are close. If the plot curves less than the data, increase the power. Otherwise decrease the power, Record your formula. Results - The formula to discover how much a bridge will bend under weight is this: b=aL3. My hypothesis (If the length of a beam or bridge is doubled, it will bend twice as much under the same amount of weight.) was rejected. If you double the length of the bridge, the bridge bends eight times as much!

Conclusions - The formula for discovering how much a bridge will bend contributes to bridge design because the formula is used in bridge design to test the safety of the bridges. This experiment is relevant because if bridges are not strong enough, they will collapse under the weight of cars or people, which could cause serious injury or death. Using this formula, one can predict how much the bridge will bend. I met my objectives by measuring the total bend of the bridge and discovering the formula for how much a bridge will bend under weight for different lengths.

Characterizing the expression and function of ADAM17a and ADAM17b in zebrafish retinal development

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Zebrafish is an excellent model for studying retinal development because the zebrafish retina is structurally and functionally very similar to the human retina. The aim of this project is to study the expression and function of ADAM17a, a member of the A Disintegrin And Metalloprotease domain family (ADAM), in zebrafish retinal development. Recent findings showed that ADAM17 participated in cleavage and activation of many important signaling pathways, such as EGFR, TNF α , and Notch. However, the functions of ADAM17, for which there are two paralogs (ADAM17a and ADAM17b), in regulating zebrafish retinal development remain unknown. As a starting point, I examined the expression patterns and levels of ADAM17a and ADAM17b using both in situ hybridization and quantitative realtime PCR (qRT-PCR) of mRNA. In situ hybridization showed that both adam17a and adam17b were first observed in the retina at 24 hpf. Additionally, adam17a and adam17b mRNA expression was detected by qRT-PCR at several time points between 0 and 24 hours, indicating that they are expressed temporally and spatially to play a role in early retinal development. To determine the function of ADAM17a and ADAM17b in retinal development, I knocked down the expression of each protein individually using morpholinos, which are modified oligonucleotides that can basepair with a target mRNA sequence and block the translation of the encoded protein. Embryos were injected with the morpholino at the 1-4 cell stage and then allowed to grow for 2, 3, or 4 days before fixation and immunostaining. The adam17a morphant retinas exhibited a significantly smaller eye size relative to the control embryos, but the adam17b morphant embryos were normal. Immunostaining of retinal sections demonstrated that both adam17a and adam17b morphant embryos displayed a change in the numbers of certain retinal cell types relative to the control retinas, suggesting that both ADAM17a and ADAM17b play key roles in development. In the future, the downstream targets of ADAM17a and ADAM17b will be investigated.

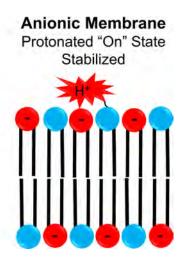
pH-responsive fluorescent probe for anionic phospholipid sensing at the membrane surface

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Surface charge on biological membranes is known to play an important role in processes such as membrane fusion and recruitment and binding of peripheral proteins. Regulation of surface charge typically occurs by changes in the expression of anionic phospholipids. Fluorescent probes are being explored as a new method of detecting changes in membrane surface charge due to the presence of anionic phospholipids. One design involved a pH-responsive pentamethine cyanine dye (Cy-5) conjugated to a phosphatidylethanolamine lipid. The probe exhibited ratiometric absorbance and "turn on" fluorescence in presence of phosphatidylserine (PS) and other anionic phospholipids. As the concentration of PS increased from 0%-50% the pKa of the probe increased by approximately 1 unit, and the fluorescence from the "on" state increased in intensity. A possible explanation for this observation is an ionic attraction between the positively charged dye and the anionic phosphatidyl serine at the membrane surface. The project is also examining other probes with different linkers to determine if there is an effect on the magnitude of the pKa shift.





Measuring the Structure of the Oxygen-16 Nucleus

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The intent of this work is to explore the structure of the nucleus of Oxygen-16 (16O), which consists of four α-particles, each with two protons and two neutrons. 16O is generated via the fusion of helium and carbon during stellar nucleosynthesis. 16O is generated via the fusion of helium and carbon during stellar nucleosynthesis. By measuring the structure of the 16O nucleus, we hope to gain a better understanding of stellar evolution and processes. The theoretical state of most interest is a linear arrangement of the four α -particles, proposed by Chevallier et al. in their 1967 paper to explain the surprisingly large moment of inertia of the nucleus they measured ¹. The existence of this state can be most accurately observed through an analysis of the energy spectra of the decay products. This method has previously been implemented at Notre Dame by Freer et al. ². A similar structure, that of Carbon-12 (12C), was analyzed, and a previously unknown state was observed. The data gathered was analyzed using the method of angular correlation, which makes use of the angles and energies of decay products relative to the center of mass frame to reconstruct possible spins of the initial state. The techniques described above are to be utilized in the 16O experiment to measure its moment of inertia. The measurements will be taken by four silicon detectors at various angles from the center of the beam line, very similar to the setup of the 2011 experiment 2, with the addition of radially arranged neutron detectors for identification of neutron-producing decay modes. By identifying the decay modes and energies of 16O and utilizing the method of angular correlations, we hope to gain new insights into the nuclear structure of 160.

References:

¹ P. Chevallier et al. "Breakup of 16O into 8Be + 8Be". In: Physical Review Vol. 160, No. 4 (August 1967), p. 827.

² M. Freer et al. "Evidence for a new 12C state at 13.3 MeV". In: Physical Review C 83 (March 2011), p. 034314.

Characterization of ACP Receptors in Anopheles Gambiae and Aedes Aegypti

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Mosquito-borne diseases cause over a million deaths each year. Two major mosquito vectors are the Anopheles gambiae, which is a major vector of malaria, and the Aedes aegypti species, a major vector of Dengue Fever and Yellow Fever. These mosquito species are developing resistance to the insecticides currently used, so it is important to develop novel insecticides to combat these diseases. G-protein coupled receptors (GPCRS), characterized by their seven-pass trans-membrane domain, play important roles in many physiological processes of mosquitoes. Therefore, they are promising candidates for insecticide development. The Adipokinetic Hormone (AKH)/Corazonin-related Peptide (ACP) receptor is a specific GPCR found in only some insects, including Anopheles gambiae and Aedes aegypti. AKH and corazonin are neuropeptides that control lipid and carbohydrate availability during flight and stressful situations. It is suspected that ACP functions like AKH, because the receptors are more structurally similar. Characterization of the ACP receptor will provide better understanding of its function and its possible use as a target for a novel insecticide. To do this, the ACP receptors of Anopheles gambiae and Aedes aegypti were cloned into a luciferase reporter construct and a stable cell line was established in human embryonic kidney (HEK293) cells. Luciferase reporter assays are used to measure cAMP levels in the cells, because changes in cAMP levels indicate GPCR signaling. Luciferase reporter assay and calcium assay results show a dose-dependent response curve. Another goal is to verify the location of the receptor, which is expected to be on the cell surface. The ACP receptors were cloned into a FLAG-tag vector, and immunostaining results will confirm receptor location.

Oral Presentation

Coxeter and Artin Group Presentations Arising from Cluster Algebras of Finite Type

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Advisor: Gregg Musiker, Department of Mathematics, University of Minnesota

I will provide an introduction to cluster algebras and discuss the classification of cluster algebras of finite type in terms of finite Dynkin diagrams. Then, after briefly discussing Coxeter and Artin groups, I will discuss a recent result of Michael Barot and Robert Marsh which describes how the Weyl group of a finite Dynkin diagram varies under diagram mutation. I will then present a generalization of this result to certain Artin groups.

The Effect of Baboon Hybridity on Parasite Resistance Mechanisms

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The effect of hybridity upon the fitness of individuals varies across species. For instance, the concept of hybrid vigor proposes that hybrid organisms benefit from outbreeding. Alternatively, hybridization may be costly if it disrupts locally-adapted gene complexes or leads to super-optimal MHC diversity that results in T-cell depletion. The baboon population in the Amboseli basin lies in a natural hybrid zone between two sub-species: yellow baboons (*Papio cynocephalus*) and Anubis baboons (*Papio cynocephalus*). Using genetic hybrid data and measures of gastrointestinal parasitism, this project hopes to explain the effect of hybridity on patterns of parasitism. We predicted that, if parasite diversity is unique to each sub-species and environment, yellow baboons may have better resistance to parasites unique to the Amboseli ecosystem and consequently have a lower parasite load compared to immigrant Anubis baboons and hybrids. In support, preliminary results suggest that in females, increased Anubis ancestry correlates with increased burden of the most prevalent and costly parasite, *Trichuris trichiura*. Further, greater Anubis ancestry again in female individuals correlates with an increased burden of *Abbreviata* sp., another relatively common and costly parasite. This study is among the first to explore the effects of hybridity on parasitism in a wild primate setting and results will have implications for understanding the selective forces that may maintain species boundaries.

Linking Decomposition to Methane Production in Alaskan Ponds

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Increasing global temperatures may enhance methane (CH₄) production in aquatic ecosystems by accelerating microbial metabolism, altering dissolved oxygen patterns, and enhancing plant growth that provides carbon for methanogens. We assessed CH₄ production in nine ponds on the Copper River Delta, Alaska via sediment incubations. To elucidate CH₄ assimilation pathways during decomposition, we provided substrate (3.0g of lily *Nuphar polysepalum*) and manipulated oxygen concentration in two treatments: anoxic and oxic. We used carbon stable isotopes to track changes in δ^{13} C of the decomposing lily substrate. The anoxic treatment had significantly higher CH₄ production rates than the oxic treatment (p<0.001). Although treatments did not differ in δ^{13} C, CH₄ production was a significant predictor of the change in δ^{13} C during decomposition (p=0.011). Changes in δ^{13} C values were also correlated with oxic methanogenesis (r=-0.73; p=0.025), suggesting that the amount of CH₄ produced limits its oxidation and assimilation during decomposition. Understanding this relationship sheds light on processes that govern an ecosystem highly susceptible to climate change and better illuminates how CH₄ dynamics impact wetland foodwebs.

Characterization of Octopamine G-Protein Coupled Receptors in Anopheles gambiae

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The spread of various diseases that affect the health of the human population are aided in their transmission through other organisms. Such vector-borne diseases can have a significant impact on the human population, especially in countries where people have little access to health care or disease prevention mechanisms. Specifically in mosquitoes, Aedes aegypti is responsible for the spread of dengue fever, rift valley fever, yellow fever and chikunguyna, while Anopheles gambiae is linked with the spread of malaria. It would be beneficial to develop an insecticide against mosquitoes that could help reduce the spread of such diseases. Currently the McDowell lab is investigating various mosquito G-protein coupled receptors (GPCR receptors) in Aedes and Anopheles that could serve as possible targets for an insecticide. GPCRs can be coupled to secondary messenger pathways, allowing them to affect many downstream pathways within the cell. For this study, two octopamine GPCRs were characterized due to the importance of this receptor in biological pathways. Octopamine can function as a neurotransmitter, neurohormone or neuromodulator in insect nervous systems as well as having a role in regulating various physiological and behavioral processes. For this reason, octopamine is a potential target for insecticides. The octopamine GPCR Anopheles 000045B (AGAP000045B) was cloned into a flag vector and transfected into HEK293 cells. The results from this study suggest that the location of the AGAP000045B receptor is on the surface of the cell. The same procedure is currently in progress for another octopamine GPCR, AGAP002519. Other lab members previously completed functional experiments to investigate the response of AGAP000045B to various agonists and similar future studies are planned for AGAP000045B and AGAP002519. Together, these experiments will help to characterize these octopamine receptors, which can hopefully be utilized in the future production of insecticides.

Refining a tool to predict antimalarial drug mechanisms of action

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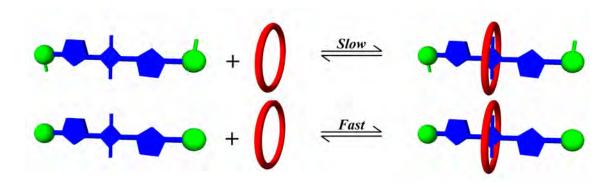
In light of developing resistance of *Plasmodium falciparum* to artemisinin and its derivatives, alternative medications are being sought after to treat malaria before current therapies become obsolete. Highthroughput screens have identified many drugs and small molecules with antimalarial activity, usually with no knowledge of their molecular targets. Cost effective prioritization of these potential drugs would be valuable to avoid pathways that have already developed drug resistance and to highlight compounds with novel mechanisms of action. We measured gene expression profiles in P. falciparum to construct a transcriptional response database for 31 drug perturbations. New drugs of interest can be queries against these gene expression patterns, identifying shared targets by similar response signatures. So far, successfully identifying drug-specific response signals has required that each gene's value be normalized across any drug perturbations from the same experiment to compute a drug's specific "response index" from myriad other experimental and biological sources of transcription variation. However, this is a cumbersome task, and we have therefore explored modifications to our approach to minimize experimental complexity while still filtering out nonspecific drug responses. We developed new protocols that can leverage existing data to specify generalized stress response signature to be used as a standard normalization with each candidate drug. Deeper analysis of the 31 drug response gene expression profiles identified a small subset of 3 drugs with highly diverse mechanisms of action. Normalization with this panel allowed removal of nonspecific culture and perturbation stress and accurate prediction of drug mechanism of action

Oral Presentation

Association Kinetics of Squaraine Pseudorotaxane Formation

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Squaraine dyes are highly conjugated and highly fluorescent dyes that emit in the red to near-IR window, which is favorable for biological imaging. However, squaraine dyes are susceptible to nucleophilic attack at their electrophilic core and degrade quickly. The Smith Group has solved this instability by encapsulating the squaraine dyes within a tetralactam macrocycle that acts as a "bullet-proof vest" over the electrophilic core of the dye. This encapsulation occurs via a reversible equilibrium as the macrocycle can slide on and off. In the "on" position, this complex is referred to as a pseudorotaxane. The pseudorotaxane retains the optical properties of the dye in addition to the increased stability. An area of ongoing study in the Smith Group is to investigate factors influencing the rate-limiting step of the formation of the pseudorotaxane. Previous studies have shown association rates are not affected by differing lengths of the R groups on either end of the dye, suggesting that the "length of the route traveled" by the macrocycle is not a factor. This project investigates the influence of simple steric differences near the dye's core. It will be shown that it is a small ethyl "speedbump" near the dye's core that is the rate-limiting factor. This presentation details the syntheses of multiple variants of methyl (no speedbump) and ethyl (speedbump) derivatives of the dye, their characterization, and kinetic measurements of encapsulation to conclude that this "speedbump" is indeed the rate limiting factor in pseudorotaxane formation.



Characterizing the Functions of ADAM10a and ADAM10b in Zebrafish Retinal Development

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Zebrafish is an excellent model to study vertebrate retinal development. Previous studies demonstrated that several genes and signaling pathways are involved in retinal development, including Notch. Notch cleavage and activation is processed by one of several A Disintegrin And Metalloproteases (ADAM) protein family members, including ADAM10. In zebrafish, there are two ADAM10 paralogs, ADAM10a and ADAM10b. This study will investigate the functions of ADAM10a and ADAM10b during zebrafish retinal development. To study the temporal expression of the adam10a and adam10b genes during development, RNA was isolated from zebrafish embryos at different time points and specific primers were used to amplify adam10a and adam10b by quantitative real-time PCR. Results showed that adam10a and adam10b mRNAs were expressed very early in development, beginning with maternal expression at 0 hours post-fertilization, suggesting that ADAM10a and ADAM10b participate in and are important in early zebrafish development. To test the function of both ADAM10 paralogs in development, newly fertilized eggs were exposed to an ADAM10 inhibitor, GI254023X. This drug treatment resulted in a significant increase in a variety of embryonic abnormalities compared to the control embryos. Immunofluorescence of sectioned developing embryonic eyes revealed greater variation the retinal cell arrangements between the GI254023X-treated embryos and the control embryos. The GI254023X-treated embryos lacked inner nuclear layer cells compared to the controls, suggesting that this retinal region either lacked cell growth or the neurons died. While these results demonstrate that ADAM10a and ADAM10b play significant roles in zebrafish retinal development, further experiments will be done to specify the roles of each protein.

Generation, Validation, and Characterization of a pax6b transgenic zebrafish line during retinal development and adult regeneration

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Advisor: David Hyde, Dept. of Biological Sciences

Millions of people suffer from visual impairments such as blindness, which can be caused by irreversible retinal cell death. Unlike humans, zebrafish regenerate lost retinal neurons to regain vision. Upon damage to the zebrafish retina, Müller glia reenter the cell cycle, produce proliferating neuronal progenitor cells that migrate to the site of damage and differentiate into the lost retinal cells. Previously, our lab showed that undamaged retinas express Pax6 in amacrine and retinal ganglion cells, but upon damage, Pax6 is upregulated in columns of neuronal progenitor cells. Quantitative PCR demonstrated that two Pax6 paralogs, pax6a and pax6b, are differentially regulated and morpholino-mediated knockdown indicated that Pax6b was necessary for neuronal progenitor cells to undergo their first cell division, while Pax6a was required for subsequent NPC amplification. To further examine the role of Pax6b in neuronal progenitor cells formation and proliferation, I generated a transgenic line using transposon-mediated BAC transgenesis that expresses GFP from the pax6b promoter. Immunohistochemistry on Tg[pax6b:GFP] retinal sections confirmed that GFP expression is confined to neuronal progenitors, amacrine cells, retinal ganglion cells, and Müller glia in both the developing and undamaged adult retina. In situ hybridization validated that the endogenous pax6b expression pattern was recapitulated by GFP expression in the Tg[pax6b:GFP] embryonic and adult retinal tissue. Additionally, pax6b splice-site morpholinos, which were injected into one-cell Tg[pax6b:GFP] embryos, significantly reduced the percentage of GFP-positive embryos relative to standard control morpholino-injected Tg[pax6b:GFP] embryos. Morpholino-mediated knockdown in adult retinal tissue also reduced GFP expression. Taken together. GFP expression in the Tg[pax6b:GFP] fish correctly mimics the endogenous expression of the pax6b gene, making this transgenic line a valuable tool for further investigating the function of pax6b in embryonic development and in the adult regenerating retina.

The influence of cover crops on soil health in Shatto Ditch Watershed, IN

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In the Midwestern U.S., tile drainage systems are commonly used to remove excess surface water from fields, as proper drainage is necessary for the production of crops. However, the tile drainage systems that maintain productive agriculture also significantly impact adjacent stream channels. Excess fertilizer nutrients like nitrogen (N) and phosphorus (P) enter streams via tile drains and are then exported downriver causing numerous problems including contaminated drinking water, harm to nutrient sensitive species, and algal blooms with subsequent hypoxia, observed in Lake Erie and the Gulf of Mexico. The planting of cover crops during the fallow period after cash crops are harvested offers a potential management strategy to reduce nutrient leaching from fields to tile drains and streams. In this project, we are studying the effects of cover crops on soil health (eg. nitrogen content, organic matter quality, etc) within agricultural soil in the Shatto Ditch Watershed, IN. We predict that the retention of nutrients during fall and spring will decrease nutrient loss during the fallow period while cover crop termination will increase nutrients available to summer crops. We also predict that planting cover crops will improve other soil health metrics, such as quantity of organic matter and level of microbial activity. Our preliminary results suggested that fields planted with cover crops had lower nitrate content in the fall and spring season, and higher nitrate content during the summer than fields not planted with cover crops. This suggested that the excess nitrate was taken up by the cover crops in the fall, retained until late spring, and then released after the cover crops were terminated in the summer. Our year-round study highlights potential benefits of the cover crop practice in retaining nutrients on fields that could otherwise be leached to surface water bodies.

Calculation of the Serial Interval of Malaria Based on Probabilistic Elements of the Transmission Cycle

John Huber College of Science

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Alex Perkins, Depts. of Applied and Computational Mathematics and Statistics and Biological Sciences, and Eck Institute for Global Health Advisor: Alex Perkins, Depts. of Applied and Computational Mathematics and Statistics and Biological Sciences, and Eck Institute for Global Health

Claiming over 650,000 lives per year, malaria exerts a serious burden on global health. While significant efforts have been made to quantify the basic reproductive number, R0, which is the average number of secondary cases arising from a primary case. However, little has been done to specify the temporal analog of R0, the serial interval. Defined as the time between successive cases, the serial interval offers an additional parameter for control efforts. In order to quantify the serial interval, probabilistic descriptions of the elements of the malaria transmission cycle were first specified as independent random variables. Then, a random variable for the serial interval was calculated by taking the sum of those random variables. We calculated the mean serial interval arising from an untreated index case to be 103.19 ± 62.63 days (mean \pm standard deviation). By comparison, the mean serial interval arising from an index case receiving artemisinin-based combination therapy with the mefloquine partner drug to be 51.30 ± 12.43 days. These values provide a benchmark estimate of the serial interval distribution for malaria. Furthermore, as a temporal analog of R0, probability distributions of the serial interval are of great utility to applications, such as efforts seeking to infer linkages between consecutive cases.

Oral Presentation

The Relationship Between Carbon Nitrogen Ratios and Chlorophyll Levels on the Senescence of Wild Blue Lupine

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Senescence is a plant adaptation that conserves nutrients through nutrient resorption. Senescence occurs in fully matured or dying leaves, where carbon and nitrogen mass-mobilize to other areas of the plant. When photosynthesis slows down, the nitrogen-storing chloroplasts disintegrate and the leaf proteins break down. Senescence is primarily a response to deteriorating environmental conditions, such as hostile temperatures, sunlight deficiency, or drought stress. We tracked the carbon-nitrogen ratio of wild blue lupine (*Lupinus perennis*) leaves harvested from the Indiana Dunes National Lakeshore to approximate the rate of nutrient resorption and senescence over a full growing season. We then compared this carbon-nitrogen rate to recorded chlorophyll rates of the same lupine plants. Preliminary results suggest that over the course of the summer, carbon-nitrogen rates and chlorophyll rates decrease similarly as senescence occurs. This data supports Buchanan-Wollaston's findings on the induction of senescence and the breakdown of chloroplasts. Once this relationship is established, we plan to explore carbon/nitrogen ratios and chlorophyll levels of the lupine in relationship to its herbivorous predator, the endangered Karner Blue Butterfly. In addition, we plan to explore how extreme weather occurrences and climate change could decouple the relationship between Karner Blue Butterfly hatching and wild lupine senescence.

Oral Presentation

Sustaining viable genetic crosses of P. falciparum through a humanized mouse model

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Genetic crosses are an effective means for the identification of genes controlling a variety of phenotypes, including drug resistance, in phenotypically distinct strains of the human malaria parasite *Plasmodium* falciparum. Although previous studies relied on the isolation of recombinant parasites from splenectomized chimpanzees, ethical and logistical issues recently prompted the National Institutes of Health (NIH) to halt chimpanzee experimentation for biomedical research. Despite 28 years of research focused on this method, only three P. falciparum genetic crosses were successfully performed during this time. In an effort to develop a new model for genetic crossing studies, a human hepatocyte-liver chimeric mouse model (FRG huHep mouse) was used to complete P. falciparum liver stage development, formation of exo-erythrocytic merozoites and transitions to asexual blood stage replication in mice injected with human red blood cells (huRBCs). Three crosses were carried out in this experiment. First, a cross was made between the documented chloroquine (CO) resistant (COR) strain, GB4, and a CO sensitive (COS) transgenic strain NF54HT-GFP-luc. Next, a cross was performed between NF54HT-GFP-luc and 7G8, a parasite used in a previous chimpanzee experimental cross. Finally a recently cloned field isolate (NHP*) was crossed with NF54HT-GFP-luc. Haplotype mapping using microsatellite markers of the 3 crosses has thus far resulted in the identification of 4, 15 and 20 unique recombinant progeny, respectively. The FRG huHep mice model harboring huRBCs has therefore proven to be a novel and versatile vehicle for experimental crosses on P. falciparum as well as an effective method of obtaining recombinant progeny for the identification of genetic determinants of parasite traits and adaptations.

A Microwell Cell-Based Assay for the Treatment of Mucopolysaccharidosis IIIA (Sanfilippo Syndrome)

Alex Im College of Science Biological Sciences

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Mucopolysaccharidosis III (MPS III), commonly known as Sanfilippo Syndrome, is a rare autosomal recessive lysosomal storage disease that primarily affects the central nervous system. MPS III is divided into four types that share similar disease pathology but are differentiated by their genetic causes and prevalence. In particular, MPS IIIA, the most common subtype, is the result of a mutated sulfamidase called heparan N-sulfatase (SGSH), a lysosomal enzyme required to degrade the glycosaminoglycan heparan sulfate (HS).

We developed a microwell cell-based assay to evaluate sulfamidase protein levels using immunofluorescence that can be measured using an automated high-content microplate cytometer. We have demonstrated a 2.62 fold difference in normalized sulfamidase levels between wild type and mutant cell lines and have demonstrated an assay with a Z-factor of 0.3559. The assay described here provides a feasible strategy for research groups or pharmaceutical companies to test a variety of synthetic molecules to identify novel compounds for the alleviation or treatment of Sanfilippo Syndrome.

On Carbon-10 Production

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Physics
James Koci
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Nuclei are known to exhibit clustering, a phenomenon in which the structure of the nucleus forms clusters resembling alpha particles. Understanding the origins of alpha clusterization is an important aspect of nuclear structure and the formation of light elements in astrophysical environments. By examining where these states exist in nuclei, we can start to understand the conditions that are necessary for the formation of these clusters. One of the places in which these cluster structures have been found is in the ¹⁴C nucleus. Due to isospin symmetry, the symmetry between a proton and neutron with respect to the nuclear force, we expect cluster structures to exist in ¹⁴C's mirror nucleus ¹⁴O. In order to look for cluster states in ¹⁴O, we will use resonant scattering of a 10C beam with a 4He target. The first step in doing this is to study the viability of producing a radioactive ¹⁰C beam using a ¹⁰B + ³He reaction. The ¹⁰C beam will separated from other reaction products using a pair of superconducting solenoid magnets called TwinSol. The production yields of ¹⁰C will be measured using a beta-decay counting station. The counting station allows for TwinSol beams to be implanted on a metal target and then radiation from the beta-decay to be counted. By measuring the amount of ¹⁰C produced with respect to other nuclei, we will determine the viability of using ¹⁰C for future resonant scattering reactions.

Oral Presentation

Damage to DNA by Atmospheric Pressure Plasma Jets with Various Oxygen Levels and Time Constraints

Andrew Jensen College of Science Science Preprofessional Studies

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Currently there are many techniques to treat cancer. One of techniques that is currently being tested is the irradiation of tumors with an atmospheric pressure plasma jet (APPJ). Because it is a new technique, the purpose of my study is to further explore the effect of APPJ on DNA. APPJs have been shown to induce both double strand and single strand breaks in DNA.1 This resulting damage to the DNA from the APPJ is due to highly reactive species, including radicals, free electrons, and ultraviolet light. Many gases can be ionized within the APPJ to create the radical species that react with the DNA. A hypothesis that different gases are associated with various levels of DNA damage has lead me to characterize the jet with respect to the oxygen and helium levels that flow into the plasma source. In addition, I have characterized the jet with respect to the duration of time that DNA is irradiated with the APPJ. These experiments were conducted using DNA solutions that were prepared using diluted 100 ng DNA in 15 μ L of deionized water. These 15 μ L solutions were irradiated with the APPJ. First, the percentage of oxygen was varied, and then irradiation time was varied. DNA was analyzed for single-strand and double-strand breaks using an agarose gel electrophoresis technique. It was observed that as both the oxygen level increased and as the time of irradiation increased that the number of strand breaks also increased.

Reference: 1. Ptasinska Sylwia, Bahnev Blagovest, Stypczynska Agnieszka, Bowden Mark, Mason Nigel J. Braithwaite, Nicholas St. J. 2010. DNA strand scission induced by a non-thermal atmospheric pressure plasma jet. Physical Chemistry Chemical Physics, 12, 7779-7781.

Surface Sterilization by Cold Atmospheric Pressure Plasma Jet

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There are an estimated 27 million surgical procedures conducted a year in the U.S. Of these approximately 500,000 lead to infection. An efficient sterilization process of surgical instruments is critical for preventing these hospital acquired infections. The usual methods of sterilization like autoclaving and chemical treatment have some disadvantages including high temperature and toxic byproducts. Instead, plasma sterilization may be a suitable alternative to conventional methods for decontamination of surgical instruments. Plasma is an electrically neutral medium composing of negative and positive particles. Plasma can be classified into thermal (hot) and non-thermal (cold) plasmas. We used a cold atmospheric plasma, which operates near room temperature, and is an effective process for inactivating microorganisms on surfaces without the need for toxic chemicals. Our present study shows the effectiveness of an atmospheric pressure plasma jet in inactivating Escherichia coli (E. coli) on Brain-Heart Infusion agar plate. Cell stocks of E. coli were prepared by incubating cultures in Luria broth and suspended to varying densities of colony forming units/ml of water. Complete inactivation of E. coli suspension treated was observed for each density. The treatment time, distance from the agar plate and helium flow rate were varied and tested for inactivation area. Plasma treatment of E. coli spread on agar plate showed that increasing treatment time increased the inactivation area, while increasing the helium flow rate decreased it and increasing the distance gave varied results. When the plasma flow was composed of 100% helium a donut shaped (ring-shaped) E. coli inactivation area was obtained, while when the composition of gas was 99.5% helium and 0.5% oxygen no ring was found in the center. Also. the pH of plasma-treated water was tested where deionized water with a tested pH around 7 was exposed to the same plasma jet for varying times and pH was immediately recorded. The plasma jet was observed to have a slight acidic effect on water decreasing the pH with increased treatment time.

The Role of EGFR Signaling in Size Homeostasis of Drosophila Embryonic Compartments

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Advisor: Jeremiah Zartman, Dept. of Chemical and Biomolecular Engineering

Understanding how organs reach their appropriate size is important for tissue engineering, and for understanding how these pathways are dysregulated in cancer. The Drosophila embryonic segments are a good model for understanding tissue size homeostasis because they are highly robust to changes in cell number. It is known that cell growth and regulation is governed by the EGFR pathway, but the specific mechanism is not well understood. One proposed mechanism involves Spitz and Ras as regulators of cell survival and therefore compartment size. These pathways can be examined by perturbing the normal cell cycle and collecting data concerning the resultant compensation in compartment size or lack thereof. Embryos genetically modified to have additional cell divisions in their anterior compartments (CycE), and wild type fly embryos were compared to analyze the differences in compartment size ratios between the two. We found that after an initial increase in the compartment size ratio difference between the CycE and wild type embryos, the compartment size ratios of the CycE embryos began to return to the wild type value. This result is consistent with the hypothesis that compartment size is regulated regardless of an extra cell division. The significance of this data is that it suggests that there is a compensation in the EGFR pathway to correct for perturbations to the normal cell cycle. Furthermore, it was confirmed through quantitative confocal microscopy of immunohistochemical assays that a gradient of EGFR signaling is present across embryonic segments, supporting the hypothesis that size control is regulated through a gradient of EGFR signaling. Further study of mutants of perturbations in apoptosis, proliferation, and EGFR signaling is needed to determine the mechanism behind this size robustness.

Oral Presentation

Dissociative Electron Attachment to Dimethylformamide

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Irradiation of molecules using low energy electrons—which are the major products of ionizing radiation—induces a fragmentation process known as dissociative electron attachment via the formation of transient anions. Amides have become a great interest in scientific research due their simplified structure, which contains a peptide linkage (O=C-N-H). As the simplest amide, formamide is capable of forming large biomolecules and several nitrogenous bases found in DNA, RNA, and nucleotide derivatives, Dimethylformamide (DMF) is a derivative of formamide and thus contains a peptide bond, which allows it to serve as a model peptide. In this study DMF was irradiated by low energy electrons. A specialized experimental high-vacuum chamber with a base pressure of 1×10-8 mbar was used in this study. Gas-phase DMF was dosed directly into the opening of the Quadrupole Mass Spectrometer (QMS) with an internal ionizer. An ion counting detector within the QMS allowed for detection and analysis of the gas phase-cations and anions in positive and negative modes, respectively. The mass spectra were used to analyze the resonances of the dominant anions and appearance energy thresholds of the cations in the energy range of 0-15eV. The anion signals were plotted as a function of electron energy using Excel and Origin software. Both the anionic species peak positions and the yield will be examined in the future and compared to known enthalpies of formation and thermodynamic thresholds to determine the stability and probability of formation. Understanding the interaction of low energy electrons with biomolecules is a progressive step towards the analysis of larger peptides and proteins.

Creating a Programming Language

Aidan Kaczanowski St Thomas The Apostle School

My name is Aidan Kaczanowski, I am in 8th grade at St. Thomas school. The title of my project is: Guis without Swing? I have spent a lot of time developing java console applications with Java Swing. During this time I noticed that it can require much effort to create a somewhat simple graphical user interface (gui). The purpose of my project is to create a programming language that will allow users to easily create aesthetically pleasing graphical user interfaces. I first decided how my programming language would function, followed by writing a parser for my language. Then I made the same gui in both my language and in Swing, and compared the code necessary. My programming language worked, but I was unhappy with the amount of control the user had over the orientation. I redesigned and rewrote my parser to allow for more control by the user from the programming language itself. After completing my language I observed that to create the gui in my language took 97 less lines of code than to do it in Swing. Therefore, my programming language creates guis much easier than Java Swing. I also believe that the difference in lines of code would increase if the complexity of the gui increased.

MT1-MMP Affects the Adhesion of Ovarian Cancer Cell Aggregates to Mouse Peritoneal Mesothelium

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Ovarian cancer was responsible for 5% of all cancer deaths suffered by American women in 2014. The overall 5-year survival rate for American women with ovarian cancer is 44%. Survival rates drop significantly when ovarian cancer is diagnosed after metastasis, as is the case in 79% of cases. Ovarian cancer that has distantly spread has a survival rate of 27%. Most women diagnosed with ovarian cancer have already experienced intra-abdominal metastasis. It is, therefore, necessary to understand how secondary metastases arise in order to develop better treatments. Ovarian cancer metastasis occurs when malignant cells or multicellular aggregates (MCAs) detach from the primary tumor site, disseminate throughout the peritoneal cavity, and subsequently adhere to mesothelium linings of abdominal organs. However, it is largely unknown what factors and molecular events regulate MCAs attaching to mesothelial cell monolayers lining the peritoneal cavity. MT1-MMP is a transmembrane collagenase that is highly expressed in ovarian cancer tumors. MT1-MMP expression has been shown to promote cellular detachment and MCA formation. Here we describe a 3D ex-vivo assay that models the interaction between the ovarian cancer cell spheroids and the mesothelial cells in vivo. We generated mutant ovarian cancer cell lines expressing wild-type MT1-MMP, T567E that mimics cytoplasmic tail Thr phosphorylation or T567A which functions as a phospho-defective mutant, and the catalytically inactive E240A active site mutant. In this study, MCAs were produced via the hanging drop method and subsequently analyzed for aggregate surface area and morphology using light microscopy. The novel ex vivo assay utilizes intact mouse peritoneum tissue to create a 3D model system. Dissected peritoneal explants are incubated with MCAs produced from different mutant ovarian cancer cell lines. This method allows monitoring both the extent and pattern of different ovarian cancer cell lines implanting in the peritoneum. Data from this experiment indicates significantly higher interaction between MT1-MMP-T567E MCAs and mouse peritoneal explants relative to cells expressing other MT1-MMP constructs. This suggests that MT1-MMP plays a role in MCA attachment to the peritoneum.

An imbalance between innate and adaptive immune cells at the maternal-fetal interface occurs prior to endotoxin-induced preterm birth

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Preterm birth is the leading cause of neonatal morbidity and mortality worldwide. A transition from an anti-inflammatory state to a pro-inflammatory state in the mother and at the maternal-fetal interface has been implicated in the pathophysiology of microbial-induced preterm labor. However, it is unclear which immune cells mediate this transition. We hypothesized that an imbalance between innate and adaptive immune cells at the maternal-fetal interface will occur prior to microbial-induced preterm labor. Using an established murine model of endotoxin-induced preterm birth, our results demonstrate that prior to delivery there is a reduction of CD4+ Tregs in the uterine tissues. This reduction is neither linked to a diminished number of Tregs in the spleen, nor to an impaired production of IL10, CCL17, and CCL22 by the uterine tissues. Endotoxin administration to pregnant mice does not alter effector CD4+ T cells at the maternal-fetal interface. However, it causes an imbalance between Tregs (CD4+ and CD8+), effector CD8+ T cells, and Th17 cells in the spleen. In addition, endotoxin administration to pregnant mice leads to an excessive production of CCL2, CCL3, CCL17, and CCL22 by the uterine tissues as well as abundant neutrophils. This imbalance in the uterine microenvironment is accompanied by scarce APClike cells such as macrophages and MHC II+ neutrophils. Collectively, these results demonstrate that endotoxin administration to pregnant mice causes an imbalance between innate and adaptive immune cells at the maternal-fetal interface.

Transcriptional Analysis of Polyamine Metabolism in Development and Disease

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Polyamines (PAs) are ubiquitous organic molecules that influence many cellular processes, including gene regulation, signal transduction, cell growth, and cell proliferation. Previous research has demonstrated that the metabolic regulation of PAs plays important roles in multiple diseases including cancer and Alzheimer's, and, moreover, that PA levels are dynamic throughout development. However, despite their multifaceted nature, the regulation and mechanistic roles of PAs remain unclear. As the mechanisms governing PA regulation and function are well conserved in animal cells, genetic studies can be done in simpler model organisms. One example is the fruit fly *Drosophila melanogaster*, which is a versatile model due to the availability of sophisticated genetic tools for investigating cellular biology and developmental genetics. Here we implement a bioinformatics approach to analyzing the transcriptional regulation of polyamine metabolism through the use of publically available gene expression data for Drosophila melanogaster. By developing a robust computational MATLAB pipeline to isolate and analyze polyamine transcriptional data from gene expression datasets of interest, we can gain an understanding of how polyamine metabolism becomes dysregulated in disease. These data will ultimately serve as a basis for a predictive ODE model of polyamine metabolism, which will provide a systems-level understanding of the process and help elucidate putative combinatorial strategies for depleting intracellular polyamines.

Regulatory gene expression in the Aedes aegypti retina

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In recent decades, there has been an alarming resurgence in vector-borne diseases like dengue and yellow fever. Understanding the visual system of the mosquito vector, *Aedes aegypti*, may provide new ways to control vector behavior and the spread of disease. The *Aedes* retina contains four distinct regions—a central region, a ventral region, a dorsal region and a ventral stripe. In this study, a protocol was developed for *in situ* hybridization using RNA probes capable of detecting transcription factors expressed in the *Aedes* retina. My goal is to characterize the developmental processes producing the four *Aedes* retinal regions. To establish the necessary experimental protocols, a control RNA probe was designed to target Aaop8, an ultraviolet-sensitive opsin known to be expressed in a large subset of *Aedes* R7 photoreceptors. PCR was performed with primers to create an Aaop8 template containing the T7 promoter sequence. This template was then used with the Roche-DIG labeling kit to create control RNA probes. The initial experimental probes will target orthodenticle, known to contribute to specification of ommatidial subtypes in *Drosophila*, and IRO-C, which is expressed in the dorsal half of the *Drosophila ommatidia*. Preliminary results indicate that a protocol, adapted from one used with zebrafish embryos, with an added SDS step for permeabilization of the retinal tissue, is effective. I report on these results and my initial efforts to assign the expression pattern of the *orthodenticle* and *IRO-C* transcription factors.

Synthesis of Dual-Ligand Probe For The Study of Niemann-Pick Type C Disease

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Niemann-Pick Type C disease is a rare, autosomal disorder that causes neurological deficits, psychological symptoms, and early morbidity. This condition is caused by a mutation in either the npc1 or npc2 gene, which code for proteins involved in the transportation of cholesterol. These proteins, NPC1 and NPC2, are well studied and characterized, but the mechanism of cholesterol transportation involving these proteins is still unknown. Cholesterol is transported into the cell in the form of low-density lipoprotein before being bound by NPC2. NPC2 is a soluble, luminal protein in late endosomes that is believed to transfer the cholesterol to the membrane protein, NPC1. NPC1 then transports cholesterol out of the lysosome via an unknown mechanism. The NPC1/NPC2 cholesterol transfer mechanism remains unknown, and the NPC1/NPC2 complex has yet to be directly observed. By designing a cholesterol-based dual-ligand molecular probe, our laboratory aims to isolate the NPC1/NPC2 protein complex. The final dual-ligand probe is constructed of two cholesterol units linked head-to-toe, with photoaffinity labels on either end to covalently bind the desired proteins. Through the synthesis of this dual-ligand probe, cholesterol-protein interactions as well as the cholesterol transfer mechanism can be further understood. We report the successful synthesis of a dual-ligand probe that, with the addition of photoaffinity substituents, can be used to stabilize this NPC1/2 complex in order to gain a better understanding of the cholesterol transfer mechanism.

Molecular profiling of aggressive breast cancer in a unique patient population from Kenya

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Breast cancer rates of incidence and mortality vary significantly between different nations and racial groups. African nations have the highest breast cancer mortality rates in the world, even though the incidence rates are below those of many other nations. In Kenya, breast cancer tumors are often highly aggressive at presentation and occur at a significantly earlier age (as early as the teens and 20s), relative to North American women. In the United States, non-Hispanic white women have the highest incidence of breast cancer, but African-American women have the highest mortality. These striking racial disparities are due not only to inequities in screening and treatment but also to variations in the rates of aggressive breast cancer. Differences in disease progression suggest that aggressive breast cancer tumors may harbor components of a unique molecular signature that result in racial disparities. We aim to identify drivers of poor prognosis breast cancer growth by identifying molecular signatures with high prognostic value from tumor samples of patients with aggressive disease. We hypothesize that changes in the DNA, RNA, and post-translational protein regulation contribute to aggressive disease. To characterize the tumors from this patient population, we used samples from >100 Kenyan breast tumor tissue samples. We stained tissue microarray sections for clinical breast cancer markers including lymphocyte markers. Using DNA and RNA that we isolated from these patient-derived breast tumors, we are characterizing these tumors by analyzing them for gene expression, genome sequencing, proteomics, and pathology analysis coupled with bioinformatics to develop signatures of aggressive breast cancer growth and metastasis. Our data will be foundational in understanding how aggressive, lethal breast tumors of Kenyan breast cancer patients differ from less aggressive tumors and will enhance our ability to diagnose and eliminate outcome disparities in breast cancer patients.

Synthesis of UV-Active Cholesterol Mimic for Study of Niemann-Pick Type C Disease

Luke Kiefer College of Science Science Business

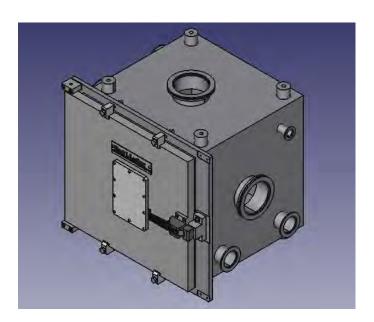
Gang Liu, Dept. of Chemistry and Biochemistry Advisor: Paul Helquist, Dept. of Chemistry and Biochemistry

KLG-1[(1R,11aR)-7-methoxy-11a-methyl-1-(5-methylhexyl)-2,10,11,11a-tetrahydro-1H-naphtho[1,2-g]indole], is a cholesterol mimic with strong UV-activity. It can be used as a biomarker for monitoring of cholesterol trafficking in situ. The synthetic pathway of KLG-1 utilizes a stereo-selective Michael addition and a reductive imine cyclization. The ability to visually study the trafficking of cholesterol has abundant potential for application in various biological pathways in which cholesterol is involved, both on the micro and macro levels. One of the various goals of monitoring cholesterol trafficking is to advance understanding of the rare disease Niemann-Pick Type C. While this disease's primary cause is a genetic abnormality in the NPC1 or NPC2 genes, the proteins that the genes code for are highly involved in cholesterol trafficking through lysosomes. The defective genes create malfunctioning proteins that are unable to transport cholesterol, leading to its accumulation and the neurodegenerative symptoms that affect those suffering from the disease. Hopefully, KLG-1 will both benefit the study of maladies resulting from deficient cholesterol trafficking and serve as a model for engineering and application of future biomarkers.

Creating a Vacuum Chamber

James Koci College of Science Physics Advisor: Tan Ahn, Dept. of Physics

The development of instrumentation in nuclear physics is crucial for advancing our ability to measure the properties of very exotic nuclei. One of the limitations of the use of exotic nuclei in experiment is their very low production intensities. Recently, active target detectors have been developed to address this issue. Active-target detectors use a gas medium to image charged-particle tracks that are emitted in nuclear reactions. This semester I have been working on designing a vacuum chamber that will be used to develop the Micro-Pattern Gas Detectors that will upgrade the capabilities of an active-target detector called the Prototype AT-TPC. I am designing the chamber through an interactive interface online through the Kurt J. Lesker Company's Chamber Builder. The design system allows me to customize a chamber that will be versatile and fit many of our group's future needs. To make sure the chamber is versatile, I have been looking at and comparing designs made by other universities and groups while tweaking specifications to create the chamber that will have a large number of ports of various size, but yet be practical. For the longer term, we would like to design and add electronics and Micro-Pattern Gas Detectors to the interior of the chamber to be able to detect charged-particle tracks from nuclear reactions with radioactive beams.



An evaluation of the relationship between self-identified race and genetic ancestry

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Advisor: Jada Benn Torres, Dept. of Anthropology

The purpose of this study is to evaluate the relationship between self-identified race and genetic ancestry within a clinical sample. In order to determine this relationship we will be examining the genetic ancestry of 75 bio-banked self-identified African American and European American females. For each sample we will sequence a portion of hypervariable region 1 (HVS1) of the mitochondrial DNA. After sequencing we will use a correlation test to quantify the relationship between the individuals' self reported race and their determined mtDNA haplogroups. Understanding this association will help reveal more about how social constructs of race may cause incongruence between how an individual racially identifies and their genetic ancestry.

When is enough, enough? Exploring potential conservation thresholds in an agricultural watershed.

Anna Kottkamp College of Science Environmental Sciences Brittany Hanrahan and Jennifer Tank, Dept. of Biological Sciences Advisor: Brittany Hanrahan, Dept. of Biological Sciences

Excess fertilizer nutrients from agricultural fields enter adjacent streams and are transported to downstream systems, causing severe environmental consequences including the recurring "Dead Zone" in the Gulf of Mexico. Planting cover crops is a conservation practice that replaces bare soil with grasses that scavenge excess N and P during winter and early spring, potentially reducing nutrient export from agricultural watersheds. Previous studies have found that cover crops reduce nitrogen export at the individual field scale. However, the practice remains uncommon; only 4% of Indiana's total land in corn/soybean cultivation was in cover cropping during 2013. Furthermore, little research has focused on the benefits of cover crops implemented at the watershed scale. Our study quantifies the water quality benefits of watershed-scale implementation of cover crops (e.g., ryegrass) planted after cash-crop harvest (i.e., corn/sovbeans). Our goal is to determine how relative cover crop coverage influences stream nutrient export in the Shatto Ditch Watershed (SDW, Kosciusko Co., IN). After cover crop planting in Fall 2013 as part of a larger study, we collected water samples and measured discharge every 14d for one year at 6 longitudinally distributed sites along 8km of stream in SDW to estimate nutrient export at each site. Using GIS and the site-specific drainage area estimated from our sampling sites, we identified nested subwatersheds (size range = 90-800 acres) within the 3000 acre SDW. We then calculated total acreage and percent cover crop coverage (range = 10-80%) in each sub-watershed and explored the relationship between stream nutrient yields (kg N/acre) and cover crop coverage. We found that metrics of nitrate export decrease as cover crop acreage increases. These results suggest a relationship between landscape cover crops and improved water quality in agricultural watersheds at small to large spatial scales, which will be useful in developing targeted conservation planning.

Oral Presentation

Merton's Portfolio Problem in a Two Asset Economy

Eric Krakowiak College of Science Mathematics

Advisors: Alex Himonas, Dept. of Mathematics and Thomas Cosimano, Dept. of Finance

A common problem nearly everyone will face in their lifetime is how to use wealth in retirement. A person would like to generate as much happiness for the remainder of their life as they can, but may be unsure how to do so. We look at an economy where a retiree has the option to spend their money, invest in a risky stock, or invest in a risk-less bond. Using stochastic calculus and dynamic programming, we find a solution for how much wealth to invest and consume over the course of retirement, and examine some interesting properties.

Periparturient relaxation of immunity in savanna baboons (Papio cynocephalus)

Julia Kruep College of Science Biological Sciences

Advisor: Elizabeth Archie, Dept. of Biological Sciences

The phenomenon known as periparturient relaxation of immunity (PPRI) in female mammals occurs when there is a decrease in energy allocated to the immune system during the post-birth period. This results in higher levels of parasitic worms and egg excretion during early lactation. The existence of PPRI has been observed in several species, including sheep and rats, but has yet to be documented in primates. In this study we looked for evidence of PPRI in wild savanna baboons (*Papio cynocephalus*) by comparing gastrointestinal parasite egg counts at differing reproductive stages. Preliminary results do not show significant differences in egg counts between reproductive states. However, there is a trend for higher Abbreviata egg counts and overall parasite abundance during lactation when compared to counts during ovarian cycling. Overall, these results improve our understanding of the costs associated with reproduction in primates.

Oral Presentation

Effects of Atmospheric Pressure Plasma on Cytosine Solutions

Emily Kunce College of Science Physics in Medicine

Advisor: Sylwia Ptasinska, Dept. of Physics and Notre Dame Radiation Laboratory

The fourth state of matter, plasmas are ionized gases that are produced when a gas is subject to a large potential difference. Plasmas contain an array of reactive species, such as: UV light, neutrals, electrons, electromagnetic fields, and ions. In recent research, plasmas have been found to selectively induce apoptosis in cancer cells. Apoptosis is controlled cell-death that minimizes trauma to the surrounding cells. As a result, these findings are promising that plasmas could be used as a potential treatment to combat epithelial cancers. An atmospheric pressure plasma jet was used to irradiate cytosine solutions to study the effects of plasma radiation. This experiment aimed to better understand the reactions that occur between plasma and the treatment solutions. H2O2 is known to be a major trigger for inducing apoptosis, so reactive H2O2 concentrations were quantified using a fluorescent dye following irradiation. After measuring up to 7 minutes of irradiation and comparing the cytosine samples to water controls, it was observed that substantial amounts of H2O2 were not produced following treatment times up to 7 minutes. After 7 minutes of irradiation, the longest treatment time, there was only a 5% difference in H2O2 concentration between the cytosine solution and water. While there was only a small difference following 7 minutes of treatment, there were sizeable differences at several of the shorter, intermediate time points. Following 0.5 minutes of irradiation, there was a 34% difference in H2O2 concentration; and after 5 minutes, there was a 16% difference. These differences in H2O2 production could be the result of the strength of the cytosine structure and the precise way in which functional groups are located within the molecules. Further studies will expand these experiments to include other nucleobases and will characterize the plasma effects.

Metabolic Transcriptome Shifting of Brain Metastatic Tumors and its Role in Metastatic Success

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Advisor: Siyuan Zhang, Dept. of Biological Sciences

Cancer metabolism has been well documented to influence primary tumor development and success; however, the role of metabolism in the metastatic tumor is not well understood. Current evidence suggests brain metastatic cells display a distinct metabolic transcriptome profile compared to their primary tumor counterparts. Here, we propose that metabolic transcriptome shifting during metastatic evolution is crucial for the metastatic success of cancer cells in the brain microenvironment. We identified a global metabolic shift in the metastatic tumor cells which includes loss of the classic Warburg effect signature. We observed one metabolic pathway enriched in the brain metastatic mature tumors compared to the mature primary tumor counterparts: the gamma-Aminobutyric acid (GABA) pathway. One gene in particular in this pathway, glutamate decarboxylase 1 (GAD1) is overexpressed in all brain metastatic tumors. We developed conditional knock-down cancer cell lines to study the role of GAD1 in multiple stages of metastatic evolution, including extravasation, colonization, and outgrowth both in vivo and in vitro. The GAD1 knock-down cancer line display fewer brain metastases and decreased proliferative potential compared to the control cancer line. To visualize the metabolic shifting in vivo, we utilized biosensors to monitor glycolytic flux and metabolic product fluctuations during early metastatic evolutionary process. First, we observe a decrease in the glycolytic flux in conjugation but a sinusoid curve of metabolic products NADH and NAD+ suggesting a decrease in glycolysis but retaining the ability to acquire energy molecules. To elucidate the metabolic flux due to GAD1 deficiency, we utilize biosensors in our knock-down cell lines. We observe a dramatic difference in metabolic flux due GAD1 deficiency. Taken together, these results suggests the metabolic transcriptome shifting decreases the majority of metabolic pathways including the Warburg effect and utilizes the GABA pathway to produce necessary metabolic products for metastatic and cellular survival.

Oral Presentation

Representation theory of the Poincare group

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Advisor: Brian Hall, Dept. of Mathematics

The Poincare group is the group of all isometries of Minkowski space-time. Studying the representation theory of this group illuminates certain symmetries of physical laws, which may be used to classify the fundamental particles that could exist by their mass and spin. We produce a description of the projective unitary representations of the Poincare group by classifying the irreducible projectve unitary representations of so-called "little groups" of the Poincare group.

Measuring urinary iodine using a paper-based test kit at parts per billion level

Ivan Leung College of Science Biochemistry

Nicholas Myers and Marya Lieberman, Dept. of Chemistry and Biochemistry Advisor: Marya Lieberman, Dept. of Chemistry and Biochemistry

The World Health Organization estimates 1/3 of the world's population has insufficient iodine intake, which leads to hypothyroidism and goiter. Even more severely impacted, infants and adolescents can develop mental and developmental impairments with insufficient iodine intake. In fact, iodine deficiency is the biggest cause of preventable intellectual disability. Conventional methods for iodine monitoring require sample preparation by boiling the urine in a strong oxidizer and monitoring of the reaction by UVvis spectroscopy. This is difficult and expensive to do in low-resource settings where iodine deficiency is most prevalent. We have developed a paper-based test that quantifies urinary iodine at parts per billion (ppb) levels without requiring any sample preparation or instrumentation at under US\$1 per sample. The device utilizes the Sandell-Kolthoff reaction, where iodine catalyzes the reduction of cerium(IV) by arsenic(III). We added ferroin, a redox indicator, to make the color change of the reaction more observable. A user can categorize samples into iodine deficient, sufficient, and excess just by the eye and obtain quantitative results with cell phone images. A blinded study, using 60 synthetic urine samples ran by two analysts on different days, showed the test has a 93% average accuracy in visual categorization. Using cell phone images, the method gave an average accuracy of 60 ppb and an inter-operator precision of 29 ppb. Preliminary data using human urine showed an accuracy of 83% (n=6) in correctly classifying the samples. Our device will be paramount in fighting iodine deficiency worldwide by providing an inexpensive way to monitor iodine intake.

A Novel Method of Relative Tumor Burden Quantification in a Murine Orthotopic Ovarian Cancer Model

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Science Preprofessional Studies and Spanish Yueying Liu, Dept. of Chemistry and Biochemistry W Matthew Leevy, Dept. of Biological Sciences

Sharon Stack, Harper Cancer Research Institute, Dept. of Chemistry and Biochemistry Advisor: Sharon Stack, Harper Cancer Research Institute, Dept. of Chemistry and Biochemistry

Epithelial ovarian cancer (EOC) is the most common cause of death of gynecologic malignancy in the United States. Given epithelial ovarian cancer's unique mode of metastasis and the fact that the vast majority of women are diagnosed with late-stage disease, optimal imaging of EOC remains of the utmost importance. Although there have been vast improvements in the ability to image tumor cells, even at the single cell level, there still exist difficulties in quantifying the metastatic tumor burden of epithelial ovarian cancer. Small animal models have proven utility in ovarian cancer research in improving our understanding of disease progression. In this experiment, we describe an optical imaging method for quantitative analysis of metastatic disease using a syngeneic orthotopic xenograft model comprised of red fluorescent protein (RFP)-labeled murine ID8 ovarian cancer cells and fully immuno-competent C57/Bl6 mice. After injection of the tumor cells, mice were imaged weekly using a Bruker Xtreme platform. At the time of sacrifice, surgical exposure of the peritoneal cavity allowed in situ imaging of the cavity's organs. The organs were then removed, placed on a labeled transparent template, and imaged ex vivo. Removal of tissue auto-fluorescence during image processing using spectral unmixing enables accurate quantification of relative tumor burden. This imaging approach possesses potential utility in future studies characterizing the effects of specific genetic, epigenetic, or micro-environmental modifications or evaluation of compounds that may inhibit metastasis of ovarian cancer and may thereby improve overall survival.

Data Analysis Pipeline for Studying Cell Signaling in Epithelial Sheets

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Advisor: Jeremiah Zartman, Dept. of Chemical and Biomolecular Engineering

Elucidating the mechanisms of growth control in epithelial tissues is important for understanding cancer and for tissue engineering applications. The *Drosophila* embryo is a good model system for size control in epithelia because it is comprises multiple segments of predetermined size along the length of the body that depend on epidermal growth factor receptor (EGFR) signaling. *Drosophilia* embryos were chosen for this research because they are easy to obtain and have a short life cycle, making it possible to maintain numerous different generations in an inexpensive manner. The *Drosophilia* genome has numerous similarities to the human genome, and therefore serves as a good model to answer questions about human tissue growth mechanisms.

Because of the large amount of data needed to test hypotheses and inform computational models, a data analysis pipeline is needed. Previously, data analysis was done by user defined segmenting, which is time consuming and leaves a large margin for user error. In order to improve the speed and efficiency of this method, the MATLAB Image Processing Toolbox was used to write an open source data analysis program which takes confocal montage data, seamlessly stiches it and allows for segmentation of individual cells and compartments.

The creation of a data analysis pipeline will allow for large amounts of data to be processed in a short amount of time, therefore providing faster and more reliable results. This data can be used to answer questions in the lab about the mechanisms that are involved in the EGFR pathway, and how they mechanisms can affect compartment dimensions and topography. Because the structures of many epithelia are similar, this pipeline will be applicable to many model systems, and also to the analysis of human samples.

Regulation of apoptosis and cell competition by hypusination in Drosophila

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Miranda Burnette, Dept. of Chemical and Biomolecular Engineering Advisor: Jeremiah Zartman, Dept. of Chemical and Biomolecular Engineering

Tumorigenesis is an extremely complicated process that relies on a symphony of signals to succeed. Our lab harnesses the sophisticated genetic tools available in *Drosophila* to identify genes functionally involved in tumorigenesis. We previously identified the *Drosophila* deoxyhypusine synthase (DHPS) homolog as a gene that increases tumor growth. Hypusination, a process requiring DHPS, is a posttranslational modification in which the amino acid lysine is altered to create the unusual amino acid hypusine. Hypusine has only been found in the protein eukaryotic translation initiation factor 5A (eIF5A), and this modification results in a functional protein vital for translational elongation, cell proliferation, and cell viability. The complete transformation of lysine to hypusine in eIF5A takes place in a two step process: an amine donation via DHPS and the addition of hydroxyl group via deoxyhypusine hydroxylase (DOHH). Inhibition of eIF5A function results in the reduction of cell size, competition, and viability. This led us to hypothesize that the hypusination pathway may constitute a novel target for cancer therapy. To test this hypothesis we used the imaginal discs of *Drosophila* larvae as a model of developing epithelia. In this model, we have generated spatially confined genetic perturbations to characterize the functional roles of DHPS in proliferation, apoptosis, and cell competition in both normal and cancerous tissues. The suppression of DHPS in imaginal discs results in a significant reduction in tissue viability and proliferation, suggesting that DHPS is essential for these processes. Further analysis of the mechanism by which DHPS regulates developing tissues will be performed. This *Drosophila* model is a currently underutilized opportunity for in vivo analysis of cell competition and apoptosis resulting from hypusination pathway mutations in a complete organism and organs. Our results are consistent with previous findings in human cells, which supports the use of a simple, easily studied organism, such as *Drosophila*, as a model to study mis-regulation of hypusination in human disease.

The Role of p-NFkB in the Intestinal Epithelium of RAG Knockout and A20 Transgenic Mice

Gordon MacDougall College of Science Science Business Charles Binghay College of Science Biological Sciences

Advisor: David Boone, Indiana University School of Medicine-South Bend and Dept. of Biological Sciences

The protein complex NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) has been shown to have a role in transcription of genes in response to a variety of environmental factors in the intestinal epithelium, including the presence of invasive microbes. The activation of NF-κB occurs via a series of cellular signals culminating in phosphorylation to phospho-NF-κB (p-NF-κB) which allows the protein complex to enter the nucleus and promote transcription of genes that code for antimicrobial peptides. Our research intends to investigate p-NF-κB's role in producing antimicrobial peptides in mice that have the RAG-1 gene "knocked out" in comparison to mice that have both the RAG-1 gene knocked out and are transgenic for the overexpression of the A20 gene, which has a role in limiting inflammation that occurs in immune responses to invasive microbes. Evidence suggests that the presence of the A20 transgene eliminates the sterility of the mucosal layer of the intestinal epithelium, allowing invasive microbes to pass through the mucosal layer and invade the epithelium, causing increased inflammation and infection of the epithelium. Through immunohistochemistry and immunofluorescence, we intend to identify the presence of activated p-NF-κB in the nuclei of the intestinal epithelial cells of mice containing the two genotypes specified above. In doing so, we can demonstrate a clear link between the activity of the A20 gene and the maintenance of sterility of the mucosal layer of the epithelium, and thereby develop our knowledge of the factors that influence colitis and intestinal distress and investigate possible treatments for related Inflammatory Bowel Diseases.

Exploring the effect of climate on the voltinism and phenology of a butterfly hybrid zone using an individual-based simulation model

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Phenology—the timing of life cycle events—and voltinism—the number of generations a population has in a given year—are predicted to be affected by climate change in insect populations. However, little is known about what impacts climate change will have on the population dynamics and selective pressures as a result of a change in the spatial variation in phenology and voltinism. Here we investigated how climate-induced changes in phenology and voltinism would affect patterns of hybridization between two hybridizing species of butterfly, Papilio glaucus and Papilio canadensis. Specifically, we examined how climate affects the phenology and potential for introgression of P. glaucus, P. canadensis and their hybrids and how voltinism may differ in warm and cool years. We used a simulation agent-based model to explore the effect of climate on their voltinism and phenology. First, three years of growth chamber data was used to test eleven development models for best fit. One model was selected based on AIC value for each life stage—egg, larvae, and pupae—and its parameters were input into the simulation model. We then tested this model with 2011 growth chamber experimental data for model validation for each treatment and stage. Next, we ran the model for various genotypes to look at the patterns across hybrid zones and predicted voltinism transition zones. Finally, we used real climate data to determine how future warming temperatures may predict large-scale phenological and voltinism patterns in the USA. Preliminary results from this work strongly suggest that changes in climate is influencing the genetic composition of this hybrid zone, by differentially affecting traits associated with voltinism and phenology in turn affecting the amount of introgression between the two species. We found that not only did climate influence voltinism patterns but hybridization may vary between warm and cool years because of the timing of emergence dates of the various genotypes.

Compatibility of 3D Printed Materials for In Vivo Optical Imaging Applications

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Three dimensional (3D) printing, or additive manufacturing, has emerged as a powerful and inexpensive platform for object creation for individuals ranging from hobbyists to scientists and engineers. Researchers across many disciplines are utilizing this technology to create parts and accessories to advance their research. One area where 3D printing is poised to make an impact is pre-clinical in vivo optical imaging. This comprises the techniques of bioluminescence and fluorescence, in which visible and near infrared light is used to non-invasively detect various biological or disease states in living mice and rats. 3D printing may be used to create a wide range of veterinary devices for stereo-tactic immobilization or anesthesia delivery, and may also be considered for applications in which an implant is utilized. However, the optical properties of mainstream 3D printer materials must be considered and properly matched to a given application. Here we report a survey of spectral profiles of 3D printable materials including ABS, PLA, Sandstone, Nylon, and Acrylic, with up to 10 colors of each type. Further, we demonstrate the practical impact of these results by creating and testing objects for primary in vivo optical imaging applications, including functional veterinary devices, optical equipment calibration units, imaging phantoms, and detectable implants. In summary, 3D printing will enable a number of advanced optical imaging applications in living mice and rats when the proper material is spectrally matched to its purpose.

Phytoplankton quality influences freshwater lake methanogenesis

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Previous research has shown increased rates of methanogenesis in freshwater sediments when additional phytoplankton biomass was amended, which allows for enhanced greenhouse gas emissions from eutrophic lakes. Despite a large literature documenting the importance of resource quality (stoichiometry or macromolecular content) for decomposition, we do not know whether substrate quality can also influence rates of methanogenesis. Our work tested whether phytoplankton substrate quality (i.e., lipid availability) or taxonomic affiliation influences freshwater lake methanogenesis. At a lab scale, we compared the effects of high and low lipid eukaryotic phytoplankton on methanogenesis in sediment from five lakes in Northern Wisconsin. Concurrently we also compared the influence of cyanobacteria and eukaryotic phytoplankton on methanogenesis rates. Our data suggest that substrate quantity had a positive effect on methanogenesis in each lake despite differing trophic status. Furthermore, we observed that phytoplankton biomass quality, in terms of lipid content, enhanced methanogenisis rates. However, we do not observe a significant effect of taxonomic affiliation (eukaryotic phytoplankton vs. cyanobacteria) on rates of methanogenesis in lake sediments when lipid content was held constant.

Addition of Channels to the Analysis Top-Quark Correlated Higgs Boson Production

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The discovery of a Higgs-like Boson by researchers at the Large Hadron Collider at CERN has proved to be one of the most significant scientific discoveries of the past decade. However, much study remains to probe the specific properties of this new particle to quantify it's resemblance to the Higgs Boson predicted in the Standard Model. One of the most important analyses, relating to the Higgs mechanism and Electroweak Symmetry Breaking, is the coupling of this boson to the top quark, which, at 173 GeV/c2, is by far the heaviest quark. In fact, the top quark mass exceeds the mass of the discovered boson (about 125 GeV/c2), so its coupling to the boson cannot be studied by a simple Higgs to top decay. Rather, this analysis focusses on gluonic Higgs production associated with a top quark pair, and the products of these particles' eventual decay. Both the Higgs and the top quark can decay into a spectrum of particles, greatly complicating matters, and this research centered on the incorporation of new decay channels into the ongoing effort to complete this analysis.

The Role of PRMT5 in Embryonic Endothelial Development and Angiogensis

Mary McDonald College of Science Biochemistry

Advisor: Joel Boerckel, Dept. of Aerospace and Mechanical Engineering

Protein arginine methyl transferase 5 (PRMT5) is an enzyme that is responsible for mono- and symmetrical dimethylation of arginine on proteins. It plays a key role in post-translational modification of growth factors, proinflammatory proteins, and transcription regulators such as HOXA9 and NFkB p65. In mice, PRMT5 total knockout is embryonic lethal between embryonic day 3.5 and 6.5, showing that PRMT5 is also important to development. HOXA9 has been shown to be an important regulator of endothelial cell differentiation and activation in addition to its role in embryonic development and hematopoiesis. Since PRMT5 is an important activator of HOXA9, it may be necessary for endothelial development.

We are investigating mice with endothelial cell-specific knockouts of PRMT5. For targeted deletion of PRMT5, we flanked PRMT5 encoding exons 2-6 with loxP sequences and inserted a premature stop codon in exon 7, resulting in loss of function of the gene. We crossed these mice against mice with Crerecombinase driven by the endothelial cell-specific Tie-2 promoter. The anticipated genotype outcomes of the crossing were ¼ heterozygous floxed without Cre (wildtype), ¼ heterozygous floxed with Cre (heterozygous), ¼ homozygous floxed without Cre (wildtype), ¼ homozygous floxed with Cre (knockout). The actual outcomes averaged across 14 litters yielded zero PRMT5 knockout pups born, and higher respective ratios of the other genotypes. We found that at embryonic day 12.5, the knockout mice were dying. To discover cause of death of the embryos, we are currently investigating the structure and size of the cardiac tissue, angiogenesis in the hindbrain, and the vasculature of the yolk sac. We are imaging Haematoxylin and Eosin stained sections of the mice embryos (harvested at embryonic days 10.5, 11.5, 12.5) to ascertain differences between the wildtype, heterozygous, and knockout phenotypes. Our findings could indicate PRMT5 as a necessary factor for endothelial cell differentiation and angiogenesis in development. In the future PRMT5 could be a new target for therapeutic strategies for pro- and anti-angiogenic therapies.

Fibroblast Oncogenic KRas Expression Induces Lung Epithelial Neoplasia via Enhanced HGF/Met Signaling

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Activated fibroblasts are found in pathological remodeling such as wound healing, organ fibrosis, and cancer. Their specific roles in these pathological events are not fully understood. To gain a better understanding of the function of activated fibroblasts in various diseases, we genetically engineered a mouse in which oncogenic KRas expression in fibroblasts is used as a surrogate for induction of their activated state (SKY mice). The mice develop lung fibrosis and progress to develop and succumb from lung adenocarcinomas over a period of 23 weeks. The activated myofibroblasts expanded from the lung of these mice expressed high levels of hepatocyte growth factor (HGF), the ligand for the Met membrane receptor. HGF signaling via the Met receptor promotes invasive growth and cellular proliferation of epithelial cells. We tested the efficacy of pharmacological inhibition of Met signaling (PF2341066) in SKY mice and noted a significant decrease in lung tumor burden following treatment. Our study highlights an important role for fibroblast-epithelial cell interactions in the emergence of lung cancer. Our results indicate that HGF production by activated fibroblast and sustained Met signaling activity in the lung epithelium promotes tumorigenesis. Future studies will test whether oncogenic KRas expression in lung fibroblast is rate limiting for lung cancer progression by treating SKY mice with deltarasin, a drug against the KRas transport protein PDEδ, and assessing disease progression. We will also explore the possible impact of lung immune infiltration on the emergence of lung cancer in these mice. Our research will help elucidate the complex relationship between fibrosis, oncogenes, and lung cancer and will aid in the discovery of potential drug targets.

Matrix Metalloproteinase-3 Impact on Primary Tumor and Metastatic Burden in Aggressive Breast Cancers

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The second leading cause of death in women, breast cancer, claims the life of over 40,000 women each year in the United States alone. The majority of these deaths occur not as a result of the primary tumor burden, but rather metastatic tumor development at secondary sites. To better understand breast cancer progression we use mouse models to study tumors and metastases in their dynamic microenvironment. Within the epithelium, cell signaling, polarity, rigidity, and adhesion are regulated through extracellular matrix (ECM) protein interactions. Uncharacteristic interactions between ECM molecules can lead to disease, and excessive proteolysis has been shown to be involved in inflammation, tumorigenesis, and abnormal cell physiology. Matrix metalloproteinases (MMPs) are zinc dependent endopeptidases whose main responsibility is to degrade ECM proteins. MMP3 is produced by fibroblasts and encourages mammary epithelial branching morphogenesis. Up-regulation of MMP3 is common in human breast cancer where it is seen in both mammary epithelial and stromal cells. Overexpression of MMP3 induces epithelial-to-mesenchymal transitions (EMT) and promotes hyperplastic growth. To investigate the localization and role of MMP3 in primary tumor progression and lung metastatic growth, we injected MMP3 or vector overexpressing cancer cells (V0PyMT) into the mammary glands of MMP3 knockout or control mice, some of which with pre-cleared epithelial. These experiments allow us to differentiate between the role of the stromal and epithelial MMP3 and revealed that this proteinase is involved in the metastatic tumor extravasation in lungs. This study will help elucidate new mechanisms through which MMP3 changes the microenvironment and ultimately encourages cancer progression and poor patient prognosis. As we understand these mechanisms we can further demonstrate the relationship between stromal processes and cancer development and can begin developing novel treatment and diagnostic options.

Use of an ecosystem-based model to predict the effects of non-native Pacific salmon spawning on stream-resident fish in the Great Lakes

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Pacific Salmon (Oncorhynchus spp.) deliver nutrients to and disturb sediments of stream ecosystems where they spawn and die, potentially altering stream organism biomass depending upon local biological, physical, and chemical characteristics of the watershed (i.e., environmental context). Little is known about how introduced salmon affect stream food web structure in the Great Lakes region, including responses of native Brook Trout (Salvelinus fontinalis) and non-native Brown Trout (Salmo trutta). To evaluate food web effects of salmon on stream-resident fish we developed a mass-balance trophic model for a typical Michigan stream using the ecosystem modeling software Ecopath with Ecosim. We ran model simulations reflecting high, intermediate, and low levels of enrichment and disturbance using values from previous studies and reflecting changes due to altered environmental context. We predicted that standing biomass of Brook and Brown Trout would decrease in response to salmon spawner presence because salmon resource subsidies are insufficient to replace invertebrate biomass lost to disturbance. Furthermore, we expected indirect enrichment through biofilm uptake to be more effective than direct enrichment through salmon egg consumption at mitigating decreased fish biomass. We found that salmon effects on stream-resident fish varied dramatically, decreasing trout biomass by ~40%, or increasing trout biomass by ~20%, depending upon the relative levels of enrichment and disturbance. Additionally, Brook and Brown Trout responded similarly to salmon spawner presence, likely due to similar diet preferences. However, both trout species exhibited stronger responses to indirect rather than direct pathways of enrichment, likely due to the persistence of indirect effects. Overall, our model provides insights about the ecological role of introduced salmon in stream ecosystems, especially with respect to stream-resident fish. This study suggests that the influence of environmental context on the balance between enrichment and disturbance should be considered when making management decisions for salmon stocking in the Great Lakes.

Multi-material 3D Printing of Multi-segmented X-ray and CT Data Sets of Mice and Rats

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The interface of 3D printing and tomographic imaging offers exciting opportunities for the observation and modeling of biological systems. Highly specific models may be produced from the reconstruction of multimodal data sets derived from CT, MRI, PET, and SPECT imaging data. These models provide accurate anatomical and molecular visualization of the 3D structure of various biological systems and are especially useful for biomedical applications, including surgical planning and research. 3D models of biological specimens are typically printed in a single primary material, limiting user ability to differentiate various aspects of the system. Our research developed a method for the segmentation, processing, and multi-material printing of multi-segmented microCT data of mice and rats. This novel methodology allowed the separate visualization of adipose tissue, soft tissue, and bone within one model. Additionally, variation in the materials used to print each tissue segmentation allowed for a more accurate representation of the actual anatomy of the specimen; bones were printed in rigid, opaque plastic while adipose and soft tissue were printed in more malleable plastic with varying color and transparency. Mice and rats were imaged using an Albira system and scanned using an HDHV, good bed scan, with 250 µm voxels. Both sets of data were reconstructed using Albira FBP software and the data was segmented based on Hounsfield unit brackets with a PMOD tool. Files were converted into 3D surface maps and repaired of their degenerate faces, open surfaces, and remaining portions of the bed. Final files were smoothed with Meshlab software and exported for printing. Models produced by the lab were accurate within 5% in any direction and the precision of the process was validated. This novel methodology established the accuracy and applications of preclinical CT and X-ray data to construct accurate anatomical models of animals in multiple materials. This process has exciting potential for the production of clinical models with anatomical CT and molecular PET imaging.



Characterization of G-Protein Coupled Receptors in Anopheles gambiae and Aedes aegypti

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The Aedes agevpti and Anopheles gambiae are two types of mosquitoes that are known vectors for diseases such as dengue, yellow fever and malaria. Vectors are organisms that host pathogens and via blood-feeding transmit the virus into their prey's blood stream. These diseases have high mortality and are a serious global health problem, especially in sub-Saharan Africa. In the past several decades there has been little progress to create an environmentally conscious and effective insecticide to prevent these mosquitoes from transmitting disease. Dr. McDowell's lab has joined the fight against mosquito vectortransmitted disease and we are beginning with signaling pathways. G-protein coupled receptors, GPCR, are protein complex of receptors that receive specified signal molecules from outside of the cell to start an intracellular signal transduction pathway cellular response. There is evidence that the serotonin gene of A. agevpti plays a role in its blood feeding behavior. Salivation is tied to blood-feeding and A. aegvpti salivation is controlled in part by serotonin release. The serotonin GPCR family is also tied to olfaction, circadian rhythm, and memory. Pharmacological characterization has been used to determine the affects of compounds different on the various serotonin GPCRs. Moreover, FLAG-tag 5-HT receptors in combination with immunostain confirm the localization of these serotonin GPCRs on the plasma membrane. If a serotonin GPCR is confirmed to be an effective pathway to target for blood-feeding suppression, it would be a major global health and insecticide industry breakthrough.

Oral Presentation

The Effect of GADD45A-Inducing Drugs in LCC versus RCC

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While left colon cancer (LCC) and right colon cancer (RCC) are treated very similarly clinically, there is increasing evidence that the two have different molecular mechanisms and progress differently as well. These differences can potentially be used both in diagnosis and treatment of colon cancer. For example, GADD45A has been identified as potential prognostic biomarker in colon cancer as it is significantly upregulated in RCC that has a poor prognosis. GADD45A's normal function in the cell is to respond to DNA damage by either initiating DNA repair or apoptotic pathways. Therefore, in general, an increased amount of GADD45A would negatively impact cancer cells as they attempt to grow. This function of GADD45A appears to be inactive in RCC as high amounts of the protein are present in cancers that grow more aggressively. To test this, a panel of four drugs whose effects include upregulated GADD45A were used on DLD-1 cells, a LCC cell line, and HCT116 cells, a RCC cell line. These drugs included 5azacytidine, genistein, trichostatin-A, and ibuprofen. The viability of these cells was then tested using a Cell Titer blue assay and the amounts of GADD45A mRNA were measured using qRTPCR. It was thought that the effects of all of these drugs would be reduced in the RCC cells as they already had increased levels of GADD45A. All four of the drugs caused a larger increase in mRNA in LCC cells than in RCC cells, but there was not a significant change in cell viability for any of the drugs between the two cells types. Future study is needed to determine how specifically these drugs affect the GADD45A pathway.

Oral Presentation

Regulation of the Oncogene ZNF217 by Localization in Breast Cancer

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Laurie Littlepage, Dept. of Chemistry and Biochemistry Advisor: Laurie Littlepage, Dept. of Chemistry and Biochemistry

Poor prognosis in breast cancer patients occurs when malignant tumors adapt to environmental insults, become resistant to chemotherapy, evade immune surveillance and metastasize to other tissues. Tumors are thought to arise from individual cells with multiple mutations, including amplification of genomic regions that provide a growth advantage. A region on human chromosome 20 called 20q13 is increased in ~25% of early stage human breast cancers and correlates with poor prognosis in patients. We have studied a novel oncogene ZNF217 within this region. ZNF217 is key in promoting breast cancer: it is not only a prognostic indicator of breast cancer progression in patients who have the worst prognosis but also is itself a drug target and/or marker of patient response to therapy. We find that ZNF217 protein is expressed most strongly in a small subset of cells within normal mammary epithelium and localizes predominantly in the nucleus of mammary epithelial cells. In contrast, the localization of ZNF217 is heterogeneous in breast tumors, with localization in both the nucleus and cytoplasm. Moreover, a truncated form of the protein localizes exclusively in the cytoplasm. We hypothesize that ZNF217 cytoplasmic localization affects ZNF217 function during cancer progression and can be used to predict poor prognosis in breast cancer patients. We have stained human breast tissue and human mammary epithelial cells for ZNF217 and find heterogeneous localization of ZNF217 across the samples. We now will identify the regions of ZNF217 that are required for ZNF217 localization in the nucleus and cytoplasm. We will utilize integrated biological approaches to determine the consequences of mislocalization of ZNF217 on cancer progression.

First AMS Results from the International Atomic Energy Agency's Intercomparison Artifacts

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Current development of local radiocarbon dating methods using Accelerator Mass Spectrometry (AMS) seeks to provide sensitive, reproducible, and accurate measurements for future interdisciplinary projects with the Biology and Anthropology departments. While AMS has been used as the premier radiocarbon dating method for a few decades, repurposing Notre Dame's FN Tandem accelerator for radiocarbon dating provides many unique challenges. Experiments showed that radiocarbon dating was possible and reproducible in the FN Tandem accelerator. As a result, a local chemistry setup was created in order to convert organic artifacts into graphite to be measured in the accelerator. There is another presentation by our group that will discuss the details of this chemistry setup. Once the setup was completed, several organic artifacts from the IAEA's radiocarbon intercomparison were procured and analyzed. With the local chemistry setup, these artifacts were converted to graphite. These graphite samples have been measured using the accelerator to determine the dates of the samples. Since the artifacts were obtained from the intercomparison, the dates obtained from the accelerator measurements can be compared to the dates from the intercomparison, providing a measure of the accuracy and repeatability of the accelerator and chemistry setup. This presentation will discuss the results obtained from the accelerator and discuss the accuracy of the current setup. Once the accelerator and chemistry setup have been proven to be accurate and repeatable, exciting projects will ensue, such as the authentication of the artwork and dating of anthropological samples.

Interaction between the gut microbiome and intestinal parasites in wild baboons

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An animal's gut microbiome, the bacteria community that inhabits its digestive tract, is an integral part to its health and survival. These bacteria interact directly with the host organism and the contents of its gut—consuming, redistributing, and storing energy. Similarly, intestinal parasites have been shown to have impacts on an animal's health, often leading to higher risks of mortality. Because parasites can reside and flourish based on the nutrients of a host's gut, and because the microbiome plays a role in digestion, it is likely that there is a relationship between the two. Parasite and microbiome data from a population of well-studied wild baboons was used to test the hypothesis that gut microbiome diversity predicts intestinal parasite load and diversity. Specifically, I predicted that the relative abundance of different bacteria would vary based on the parasite load and which parasite species were present. Preliminary results show that microbiome alpha diversity, the number of bacterial taxa present, can be influenced by the absence/presence of certain parasites, whereas microbiome beta diversity was not. In particular, the parasite *Trichuris trichiura* was shown to affect the alpha diversity of the microbiome. The data from this experiment will provide a foundation for understanding the relationship between the microbiome and parasites in wild animals.

Analysis of Blastocystis Parasites in Macaca fascicularis

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Blastocystis is a globally distributed stramenophile parasite that is of major importance as an opportunistic pathogen of the immunocompromised, and has been implicated as a causal agent of irritable bowel disease. However, little is actually known about the transmission dynamics of this parasite in wild populations. Zoonotic transmission is believed to be a major contributor to human *Blastocystis* infections. Studies on Blastocystis transmission in wild-animals are thus essential to understanding the sources of Blastocystis infection. This research explores the factors affecting Blastocystis population structure and transmission in Macaca fascicularis (long-tailed macaque), a useful model organism for investigating parasite population dynamics, as it could act as a potential reservoir for *Blastocystis* due to its close interface with humans. This project investigates the host population genetic structure in addition to environmental and anthropogenic variables in Singapore and Bali in order to determine factors that influence Blastocystis transmission and persistence. Analysis of the parasite's allelic richness and community composition was completed using *Blastocystis* sequence data extracted from fecal samples collected from 23 sites in Bali and Singapore in 2011. Preliminary results indicate that host mitochondrial DNA did not predict parasite population structure. Isolation by distance did not occur in Singapore or Bali, but structuring was detected between the two islands. This study also indicates that host population size and proximity to urban areas are factors that affect Blastocystis, as well as a relationship between increased *Blastocystis* allele richness and larger macaque population size, a factor directly influenced by humans through feeding. This implies human activity is a contributor to Blastocystis transmission and genetic structure. This study suggests that management of the human macaque interface may be effective for reducing the threats of zoonotic disease.

Potential Mediators of Childhood Exposure to Violence and Health Problems in Young Adulthood

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While much research has been done to show the impact of childhood trauma exposure on the physical health of young children and adults, it is still unclear how exposure to violence at a young age affects the health of college-aged students. We hypothesized that children exposed to trauma will show higher levels of physical health issues, and that this relationship is mediated by higher stress levels among this population. Participants included 385 college students from the Universities of Memphis and Notre Dame with a mean age of 19.22. Our analytic methodology showed, through a multiple regression analysis, that physical health issues were strongly correlated with experiences of childhood trauma. Moreover, the mediation of stress was significant in this relationship. Gender difference also played a significant role, however the two factors did not interact in a meaningful way. The support of our hypothesis shows the potential for improved identification and treatment of college students struggling with the physical effects of childhood trauma. These findings provide an opportunity for advanced intervention efforts that can work to enhance college communities by targeting the stress experienced by this population. Such intervention would strengthen college communities and promote the overall well-being of students.

Oral Presentation

The Role of Coagulation and Platelet Dysfunction in a Rat Model of Traumatic Brain Injury

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There are ~ 1.7M reported cases per year of traumatic brain injury (TBI) in the United States with approximately 50,000 deaths, ~230,000 hospitalizations and survival, and ~85,000 that suffer long-term disability. A potential cause for this mortality and morbidity is the development of coagulopathy. Coagulopathy is a condition in which the blood's clotting process is dysfunctional and can lead to delayed healing and prolonged bleeding after injury. It is a complication of traumatic brain injury (TBI), and recent studies have implicated platelet dysfunction in response to agonists adenosine diphosphate and arachidonic acid as a component of dysregulated coagulation. The mechanism by which platelet dysfunction arises is poorly understood, but the recent development in our laboratory of a rodent model of TBI that mimics the coagulopathy observed clinically can aid in its elucidation. In this study immunohistochemistry was used to show the expression and localization of coagulation and platelet activation markers in post-traumatic rat brain. Enhanced localized Tissue Factor (TF) and platelet activation marker, P-Selectin, were observed in the brain early after trauma. These results paralleled alterations in systemic platelet responsiveness to adenosine diphosphate and arachidonic acid. Additionally, increased circulating TF microparticles and thrombin/antithrombin (TAT) complex were enhanced, post-injury, indicating activation of the blood coagulation system and potentially early activation of platelets with resultant platelet exhaustion. This would indicate that isolated brain injury has a global effect on the systemic coagulation cascade and platelet function.

Splenda and Sulci: A Critical Review of the Effects of Artificial Sweeteners on Cognitive and Neural Functioning

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In recent years, significant controversy has emerged in both scientific and popular cultures regarding the health effects of artificial sweeteners. While in theory artificial sweeteners can reduce consumption of caloric sugars, potentially leading to weight loss and a healthier lifestyle, the long-term effects of artificial sweeteners on the body and the brain need further examination.

Numerous studies have shown that non-nutritive sweeteners, especially aspartame, can have negative cognitive and physiological consequences in human beings; however, other studies on aspartame and non-nutritive sweeteners show evidence that no significantly-detrimental effects result from artificial sweetener consumption. So how do artificial sweeteners actually affect the brain and cognition? In this literature review, I will explore the current literature on artificial sweeteners to gain a better understanding of the effects of non-nutritive sweeteners on brain development and function, focusing more heavily on artificial sweeteners that have not received extensive attention. Ultimately, the aim of this review is to sort through the current divisive research on artificial sweeteners, to explore the effects of artificial sweeteners on human health and to suggest further directions of study regarding artificial sweeteners and the nervous system.

Oral Presentation

Exploring the use of Zn-BDPA's as adjuvants for the cellular uptake of 5-ALA

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The naturally-occurring fluorophore protoporphyrin IX (PPIX) has been approved by the FDA for use in photodynamic therapy (PDT) of certain epithelial cancers. Additionally, current research has demonstrated that it increases the success of resection of malignant gliomas when used in fluorescenceguided surgery. This is possible through its high selectivity for cancerous tissue, when administered locally as well as systemically. PPIX and 5-aminolevulinic acid (5-ALA), a hydrophilic pro-drug for PPIX, have been shown to differentially accumulate in cancerous versus non-cancerous tissue in vivo, with greater accumulation in cancerous tissue. However, accumulation in non-cancerous tissue results in residual photosensitivity, and patients must often remain protected from light for days after treatment. Many approaches have been taken to increase cellular accumulation of PPIX, including synthesizing more lipophilic ester derivatives of 5-ALA, synthesizing PPIX oligomers, and targeted drug delivery using nanoparticles. In this study, we explored the use of zinc(II)-bis(dipicolylamine) (Zn-BDPA) molecules as potential adjuvants to facilitate 5-ALA entry into CHO-K1 cancer cells in vitro. Using fluorometry, fluorescence microscopy, and flow cytometry assays, we were able to measure the fluorescence of PPIX and determine the efficacy of each treatment in increasing 5-ALA uptake. After testing a library of Zn-BPDA compounds, we have identified 10uM tyrosine Zn-BDPA as the most effective adjuvant to 100uM 5-ALA, with over a threefold increase in PPIX accumulation and negligible toxicity, relative to treatment with 100μM 5-ALA alone. Furthermore, addition of tyrosine Zn-BPDA results in accumulation of PPIX at lower concentrations than possible when treating cells with 5-ALA alone. Mechanistic studies examining binding between tyrosine Zn-BDPA and 5-ALA, competitive inhibition of 5-ALA entry into cells, and cell membrane integrity suggest that the tyrosine Zn-BDPA molecule temporarily permeabilizes the cell membrane, allowing the hydrophilic 5-ALA to cross the membrane, without causing cell death. Future work will investigate tyrosine Zn-BDPA as an adjuvant in other contexts, such as transfection. In vivo studies may also demonstrate tyrosine Zn-BDPA as a viable clinical adjuvant for uptake of 5-ALA or other drugs.

Analyzing a Supersonic Helium Jet Gas Target for Nuclear Astrophysics

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St. George is a Recoil Mass Separator at The Nuclear Science Laboratory at the University of Notre Dame. It is used to study nuclear reactions that take place in the core of stars. The separator is equipped with a helium jet gas target in which the beam of the St. Ana accelerator interacts. The jet gas target injects helium gas at supersonic speed in the path of the particle beam. The injected helium is then quickly pumped out of the beam-line to maintain the vacuum state as close to the target as possible. What is not known are the dimensions of this bulge. Currently, the aerodynamics of the nozzle is being studied to define the behavior of the gas as it flows through and beyond the nozzle. These initial calculations will be used to perform computational fluid dynamics analysis of the gas target. The goal of the calculations and analysis is to determine the current state of the bulge after the nozzle, and eventually to redesign the nozzle, and possible the target, to control the shape and location of this bulge to better manage the particle interactions.

Elucidating the importance of a nonribosomal peptide synthetase in Mycobacterium marinum

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Tuberculosis is a human disease primarily caused by *Mycobacterium tuberculosis*. To develop drugs to fight against Tuberculosis, it is important to identify genes involved in virulence. We are using a model species, *Mycobacterium marinum*, to understand mycobacterial virulence at the genetic level. From a list of potential Esx-1 deficient mutant strains provided by a MALDI screen and an amoeba screen of an *M. marinum* transposon-insertion library conducted by the Champion lab, I identified strain 113H4 and confirmed it was lacking a known virulence pathway, the Esx-1 secretion system. I mapped the transposon to *MMAR_3271*, a gene that encodes for a putative nonribosomal peptide synthetase (NRPS). NRPSs are modular enzymes that make natural peptide products in the absence of the ribosome. Interestingly, this locus was also identified in an additional transposon strain. Genetic complementation for this mutant strain was achieved by adding in a second copy of known Esx-1 genes. These findings may indicate that the transposon insertion in the NRPS may not be causing the Esx-1-deficiency. However, a recent study by the Bitter lab identified this locus as important for virulence. Future directions will focus on determining 1) if the NRPS locus is important for virulence in an Esx-1-dependent or independent manner and 2) the natural product made by this NRPS through biochemical and genetic approaches. This project can provide scientific insight on the biology of *M. marinum*.

Variation in metabolic rate and salinity tolerance within a population of Daphnia pulex

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Genetic variation produces phenotypic traits on which natural selection acts, resulting in evolution. To understand this mechanism in a population, we need to know how much genetic variation there is, what the sources of those are, and how they change over time. In our study, we used a population of *Daphnia* pulex collected from Eloise Butler (EB) Lake located in Minneapolis, MN. 100 individuals were then resequenced in order to examine genetic variation within the population, with the goal of examining how much phenotypic variation exists within the EB population. *Daphnia pulex*, a freshwater invertebrate, shows high plasticity and has a short generation time (~ 10 days). Therefore, they make good organisms for testing short and long-term biotic and abiotic treatments on and they are a good model organism for ecology, toxicology, and genetic studies. Metabolic rates and salinity tolerance were chosen as phenotypes of interest. First of all, we measured oxygen consumptions and used calculations to find the metabolic rates of each Daphnia sampled. Oxygen consumption can show us how different genotypes of Daphnia behave in similar anoxic environments. Anoxic environments may be due to pollution by chemicals, by nutrient runoff or through eutrophication by algae blooms. We also looked at salinity tolerance of *Daphnia*. Salinity tolerance can show us how certain clones of *Daphnia* will cope, as opposed to other clones, when in saline environments. Previous studies have shown that different genotypes exhibit a wide range of salinity tolerance. Our results showed that there is a significant amount of variation in phenotypes within the EB population. For subsequent studies, we plan on collecting more phenotypic data, such as migration patterns, and examine the relationship between phenotypic and genetic variation within a population.

Proteins that Determine Destination in RNA Localization

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Movement of mRNA to specific intracellular locations underlies several important biological processes; most notable are the development of asymmetric embryos from a single cell, the positioning of signaling machinery at neuron synapses, and the formation of cellular projections for cell movement. In the majority of cases, RNA localization depends on the binding of protein factors to a sequence element in the RNA. Several of the proteins involved in RNA transport in *Xenopus* oocytes have been identified and an interaction map has been constructed. We have determined that hnRNP U interacts with the protein Staufen and is a likely component of the protein complex that directs the localization of mRNA in the oocyte. Despite evidence that it may determine the direction of RNA movement, a functional role for hnRNP U has not been documented. Fluorescently labeled (Alexa Fluor 488) Vg1 mRNA, which localizes solely to the vegetal hemisphere, is synthesized by run-off transcription and then microinjected into stage III oocytes. The position of Vg1 mRNA is visualized using confocal microscopy. The function of the hnRNP U protein is being tested by co-injection of Vg1 mRNA with an antibody that binds to, and thus masks, hnRNP U. The inhibitory effect of the antibody has provided the first evidence that hnRNP U is a necessary factor for RNA localization. Current experiments are testing the effect of the antibody on An1 mRNA, which moves to the opposite, animal, hemisphere and does not bind to hnRNP U.

Nickel-Catalyzed Halogen Exchange of Vinyl and Aryl Halides

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Michael Grigalunas, Dept. of Chemistry and Biochemistry Advisor: Paul Helquist, Dept. of Chemistry and Biochemistry

Vinyl and aryl halides are common synthetic intermediates in organic synthesis. These functionalities are contained in a wide range of substrates, particularly precursors for transition metal-mediated couplings. Both functionalities also possess utility as sites for radiolabelling in medical imaging. Iodides are commonly the most reactive of these substrates, but are not as readily available. Developing new methods for exchanging iodide for more available bromide and chloride structures under mild conditions is an outstanding issue. While investigating a nickel catalyzed α -alkenylation reaction, our lab discovered new conditions for a nickel-mediated halogen exchange. Subsequent work has focused on optimizing this process and examining the scope of the reaction. Possible applications in other couplings and synthesis are also being investigated.

Kinetic Study of a Classical Oxygen Atom Transfer Reaction and Characterization of an Unstable Intermediate

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In order to further the understanding of classical and non-classical oxygen atom transfer (OAT) reactions, the kinetics of the reaction between $MoO_2(oxine)_2$ and dimethylphenylphosphine were studied across a variety of temperatures and concentrations. These kinetics indicated that the rate of reaction for a similar non-classical OAT reaction to be significantly faster by comparison. The tungsten analogue $WO_2(oxine)_2$ was also successfully prepared and characterized. However, the low solubility of this complex hindered its kinetic study. In addition, steps taken towards the isolation of the unstable intermediate in the reaction of (Clip)MoO(pyr) with N-Methylmorpholine N-oxide will be discussed.

Targeting polyamine pathway activity in Drosophila Tumorigenesis

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Polyamines are polycationic molecules with pleiotropic roles in cellular processes. In particular, they have been implicated for roles in tumorigenesis and the development of certain tissues. Tumors exhibit increased polyamine biosynthesis, and there is accumulating evidence for roles for polyamines downstream of oncogenes. Thus many attempts have been made to pharmacologically target polyamine biosynthesis as an anticancer therapy. Unfortunately, efficacy of such treatments has been limited by the efficiency of the polyamine regulatory system, for example increased polyamine uptake in response to cellular polyamine depletion. Based on these findings, there is a great need to target polyamine transporter genes in parallel with polyamine depleting therapies. However, little is known about the identity of mammalian polyamine transporters. Here we use an in vivo tumor model system with RNA interference (RNAi)-mediated knockdown of candidate polyamine pathway genes to identify novel effectors of polyamine activity in cancer using the fruit fly, *Drosophila melanogaster*. Using a secondary, wild type model we can analyze the effects of candidate genes on normal development. Due to the high level of conservation in the polyamine pathway between *Drosophila* and humans, genes confirmed as having roles in tumor formation and progression in *Drosophila* can provide promising new leads for the next generation of cancer therapeutics.

Increased Calcium Results in Decreased Swarming Motility of the Bacteria Pseudomonas aeruginosa

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Pseudomonas aeruginosa is a ubiquitous bacterium that is recognized as an opportunistic pathogen that causes infections in immunocompromised individuals. Pseudomonas aeruginosa infections in the lungs of Cystic Fibrosis (CF) patients are chronic and difficult to treat. These bacteria produce a dense recalcitrant biofilm in the CF lung, rendering many antibiotic regimens unsuccessful. These infections are well classified, but little is understood about the environmental cues for P. aeruginosa behavior during the transition from the environment to human host. Understanding this transition may allow for prevention and improved treatments of P. aeruginosa lung infections. It has been shown that calcium affects bacterial attachment, the structure of biofilms, and secretion of virulence factors, but little is known about the effect of calcium on motility. Increases in calcium concentrations were found to decrease swarming motility in a clinical CF isolate of P. aeruginosa. While swarming requires flagellar motility, appendages called type IV pili have recently been shown to influence flagellar mediated swarming. Collective results from these experiments suggest that calcium affects both flagellar and type IV pili function during swarming. As both flagella and type IV pili are important to attachment of P. aeruginosa to surfaces, our results correspond with other studies showing increased calcium increases bacterial attachment. Future studies aim to isolate the calcium effect on type IV pili production and function by generating a mutant strain that can only exhibit type IV pili motility. Twitch assays will be carried out on this mutant strain to characterize how calcium affects twitching motility. Understanding the calcium effect may uncover potential targets for treating chronic P. aeruginosa infections.

Oral Presentation

Dark-adaptation-mediated rod precursor cell proliferation in the adult zebrafish retina

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Zebrafish exhibit persistent neurogenesis throughout their life and neuronal regeneration following insult or injury. Retinal rod photoreceptors are produced from Müller glial-derived rod precursor cells that are committed to only differentiate into rods. Damage to rods induces either Müller glia proliferation or rod precursor cell proliferation, both leading to rod regeneration. In light-damaged retinas, rod precursor cell proliferation is followed by Müller glia proliferation. We demonstrate that this rod precursor cell proliferation may not be a response to light-induced rod cell death. There is no significant difference in the number of rod precursor cells in both undamaged and light-damaged retinas that were previously dark-adapted. However, undamaged dark-adapted fish possess significantly greater numbers of proliferating rod precursor cells relative to fish maintained in standard light conditions. This suggests that prolonged dark-adaptation induces rod precursor cell proliferation, rather than light-induced rod photoreceptor death. An EdU/BrdU pulse chase experiment revealed that rod precursor cells are recruited into the cell cycle during dark adaptation. We investigated whether cell death, Müller glia proliferation, or neuronal progenitor cell proliferation were involved in the dark-adaptation response. Similar numbers of TUNEL-positive cells were present in the photoreceptor layer throughout the dark-adaptation timecourse, suggesting that cell death was not stimulating increased rod precursor cell proliferation. Moreover, the number of proliferating Müller glia and neuronal progenitor cells were assessed in Tg[gfap:EGFP] and Tg[olig2:EGFP] zebrafish, respectively. Both proliferating Müller glia and neuronal progenitor cells were statistically increased throughout the dark-adaptation timecourse suggesting neither population gives rise to increased rod precursor cell proliferation. In conclusion, dark-adaptation induces rod precursor cell proliferation through a mechanism that is independent of either cell death or Müller glia and neuronal progenitor cell proliferation.

Sequential Analysis of 2009-2013 American Time Use Survey Data

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Time use research is an interdisciplinary field that aims to understand how individuals spend their time over a specific amount of time. It is a developing field that promises important insights. One particular area of time use research is sequence analysis, which is the study of the series of events that typically happen over a given period of time. This research project provides a sequential analysis of the American Time Use Survey data from the years 2009-2013, using optimal matching methods. Optimal matching (OM) is a popular method for examining sequential social science data. OM's purpose is to measure pairwise dissimilarities between sequences, using defined "costs" to transform one sequence to another. The resulting matrix is then analyzed in a clustering algorithm in order to build a typology of the observed sequences. OM is currently the most popular approach for sequence analysis. This research seeks to explore the effectiveness of OM in sequence analysis of the ATUS data. OM methods provide compelling insight into the ATUS data set, especially in combination with descriptive statistic and data visualizations. Using visualizations completed by the package TraMineR in R, an overview of the sequences and structure present in the ATUS data set is provided. These statistical methods and visualizations are helpful in illuminating trends in how individuals allocate their time over the period of a day. This information is necessary and can be effective in areas such as public policymaking, regarding urban design, transportation planning, recreation and active living, or economics. Comparing ATUS data over several years can also provide insight into the effectiveness of certain policies (such as those that encourage physical activity). Further research may include refining the techniques used here or comparing OM to other popular algorithms.

Anatomical Imaging of Thioacetamide Induced Liver Damage in Mice with Magnetic Resonance

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Biochemistry and French
Sarah Chapman, Dept. of Biological Sciences
Advisor: W Matthew Leevy, Dept. of Biological Sciences

Liver fibrosis is a disease caused by chronic liver damage that can result in cirrhosis, liver failure, and liver transplantation. Thioacetamide (TAA) is a hepatotoxic drug that induces liver fibrosis and is widely used as a model of liver failure, which results in the loss of hepatic function. Through a hepatocyte absorption mechanism. TAA induces an accumulation of toxic metabolites that cause cell damage and ultimately death of the liver. While TAA has been used extensively for mouse models of liver damage, there is little literature on using anatomical imaging, such as computed tomography (CT) and magnetic resonance (MRI), to visualize and quantify the liver failure due to drug overdose. In order to advance the protocols for examination of the effects of TAA, this study aimed to determine a viable imaging strategy for liver damage in mice and to use these techniques to quantify these anatomical changes. While our studies found that CT did not provide anatomical evidence of liver damage, preliminary MRI studies demonstrate higher resolution liver images with signs of TAA-induced damage. Here, we present the methods used to visualize the mouse liver with an MRI T1-weighted fast low angle shot (FLASH) sequence in order to examine the effects of TAA on the soft tissue. Future research may incorporate different MRI techniques in order to determine the best image acquisition methods for liver resolution as well as examine different organ systems in order to assess TAA organ damage on a more comprehensive level. These results will provide researchers an alternate imaging modality for evaluating the TAA liver damage mouse model.

Expression of MT1-MMP Affects Epithelial Integrity in Epithelial Ovarian Cancer

Kristal Quispe College of Arts & Letters Psychology

Jing Yang and Sharon Stack, Harper Cancer Research Institute and Dept. of Chemistry and Biochemistry Advisors: Sharon Stack and Jing Yang,

Harper Cancer Research Institute and Dept. of Chemistry and Biochemistry

Epithelial ovarian cancer (EOC) is the fifth leading cause of cancer deaths among women. According to The American Cancer Society, there will be an estimated 21, 290 new cases of EOC diagnosed in 2015, resulting in 14,180 American deaths. These alarming statistics highlight the need to develop early detection methods and a better understanding of the molecular interactions leading up to metastasis. Ovarian cancer cells are present in malignant ascites both as individual cells and as multicellular aggregates (MCAs), through a metastasis process that occurs via a unique anchorage-independent mechanism. Previous studies have shown that acquired MT1-MMP expression promotes cellular detachment and MCA formation. The MMP proteases are a family of zinc dependent enzymes and are able to degrade extracellular matrix proteins, while a membrane type 1 MMP (MT1) is a transmembrane collagenase that is over expressed in EOC tumors. In this study, we generated mutant ovarian cancer cell lines expressing wild-type MT1-MMP, T567E that mimics cytoplasmic tail Thr phosphorylation, or T567A which functions as a phosphodefective mutant, and the catalytically inactive E240A active site mutant. Here we focus on evaluation of cell-cell cohesion and cellular detachment among different ovarian cancer cell lines. A loss of cell-cell cohesion is prevalent and an indicator of tumor metastasis. The effect of MT1-MMP on cell-cell cohesion was analyzed via a dispase-based dissociation assay, which examines the relative resistance of epithelial cell sheets to dissociation into single cells. Our data suggest MT1-MMP plays a role in modifying epithelial integrity, thus potentiating ovarian cancer metastatic dissemination.

Aquaponics Across the Spectrum: Bridging Science Education to STEM-Based Careers and Eco-Stewardship

Shella Raja College of Science Biological Sciences Advisor: Susan Blum, Dept. of Anthropology

There are nourishing social, psychological, and physical health benefits of gardening across all ages, abilities, and cultures. Aquaponics is a form of sustainable agriculture or gardening that is growing in popularity around the world. It involves the low-impact cycling of nutrient-rich water from a fish tank to the root systems of plants without the need for soil. Green Bridge Growers of South Bend, IN has demonstrated that young adults with autism thrive when working in an aquaponics setting. An effective method that can be used to spread the knowledge and benefits of aquaponics to students is through STEM-based education. Inclusivity of all students within STEM education can be enhanced by tailoring an aquaponics program for both students with autism spectrum disorder and "neurotypical" students. This would not only stimulate an active dedication to STEM fields and food security, but would also create an environment of acceptance and growth for all who participate. Aquaponics Across the Spectrum was designed by a team from St. Mary's, Notre Dame, and Green Bridge Growers. It is meant to be an eightworkshop, after-school program but has been compressed into five workshops for implementation at Edison Intermediate Center in South Bend, IN between March and April of 2015. We are utilizing iPad technology as well as traditional school supplies during the workshops. We have volunteers from both St. Mary's and Notre Dame to help teach the curriculum, which features activities in sustainability, aquaponics, and plant and fish needs. It also includes the building of miniature aquaponics demo systems in groups of two students. At the conclusion of the program, students will present their demos to friends and family in a science fair format. The products of this program include a website, blog, and curriculum. Future repetitions of the program will improve upon the pilot trial. This is the product of a sustainability minor's senior capstone project. It was funded by ISLA and the College of Science.

Bacterial protein half-life analysis

Robert Reed College of Science Biological Sciences

Advisor: Stuart Jones, Dept. of Biological Sciences

Bacteria are the most abundant and diverse organisms on the planet, and like other organism, they are able to take in and transform nutrients and biomass into biologically useful energy. Mediating the acquisition of nutrients, proteins in the cell also allow for acclimation to environmental changes. As all organisms do, bacteria balance the creation and breakdown of proteins. The rate that bacteria breakdown their own proteins is critical to understanding their responsiveness to environmental changes. By a colorimetric assay, we measure the protein degradation for several strains at different time points after arresting the protein production to prevent further growth. We estimate the protein half-life based on the protein degradation. Preliminary results show differences between the strains thus far analyzed. Considering protein turnover to be an energy consuming process, in the future, we want to associate these results with a bacterium's growth efficiency and flexibility.

Bitter and Twisted: Analysis of Diet and Torsional Resistance in the Mandibles of Strepsirrhine Primates

Vincent Riccelli College of Science Biological Sciences Anna Szentirmai College of Science Biological Sciences

Advisors: Matthew Ravosa, Dept. of Biological Sciences and Christopher Vinyard, Dept. of Anatomy and Neurobiology, College of Medicine, Northeast Ohio Medical University

Morphological and experimental analyses in strepsirrhine primates suggest that mandibular robusticity results from chewing and biting of mechanically demanding diets. Oral processing of hard and tough items is believed to impart torsional stresses to the mandibular corpus due to a combination of bite and muscle forces. However, most of the comparative evidence for such conclusions is based on external mandibular proportions, which do not always reflect the biomechanical characteristics of the lower jaw. Using novel data on the internal anatomy of the mandibular corpus, we evaluate the influence of diet on torsional resistance in strepsirrhines and compare torsional resistance to geometric variables related to bending and shear resistance. Our sample consisted of 82 adult mandibles from 29 species with diverse diets, which were imaged via microCT to obtain cross-sectional dimensions at three premolar (P2, P3, P4) and three molar (M1, M2, M3) sections. Log-linear bivariate regression controlling for phylogenetic relatedness (p<0.05) was used to perform standard allometric comparisons between mandible length and torsional resistance, measured using Bredt's formula (K) at molar and premolar sections of the corpus, and residuals were correlated with dietary composition. K scaled isometrically in strepsirrhines for all six sections, as did variables related to bending and shear resistance of the mandibular corpus, indicating that jaw-loading regimes do not appear to change with size. In all sections, residuals from bivariate regressions were related to the percentage of diet composed of hard and/or tough foods such as bamboo, seeds and leaves. This indicates that jaw cross-sectional robusticity in strepsirrhines is linked to the processing of foods that require repetitive and/or forceful chewing and biting. Our study also suggests that, in addition to elevated bending and shear, mechanically challenging diets impart significant torsional stresses on the mandibular corpus and that this influences the internal anatomy of the strepsirrhine jaw.

Flavorful Memories

Joseph Rice St Thomas The Apostle School

For my project I wanted to find out if you chewed gum while studying information, and that same flavor gum while taking a test on that information, would your scores improve versus ones who didnt chew gum. My hypothesis was that your scores would have a higher improvement in the group that chewed gum opposed to the group that didn't chew gum. My research, which showed me that similar studies I saw online, backed this. I made a designated slide show with 20 world landmark pictures with no labels and the same 20 with labels. Then, I showed volunteers the first 20 pictures with no labels and they wrote their answers for what they were. I divided the volunteers into two groups, one that chewed gum while studying and the other didn't. Then, I went over the slide show answers, and each person studied for five minutes. I then waited the rest of that day and two additional days. I made a second test with the same 20 pictures, but in a different order. After the waiting period, I gave the non-gum group and the gum group the test. When they finished, I took the tests and found the individual improvement and the group improvement versus the first test. The results showed group one had a higher improvement average. I can conclude that chewing gum while studying and the same flavor while taking the test doesn't improve the score, but may decrease them.

Surface-enhanced Raman detection of carbohydrates

College of Science
Advisor: Zachary Schultz, Dept. of Chemistry and Biochemistry

Raman spectroscopy is a useful analytical tool for biomolecular characterization. Differences in the structure of glycans, or carbohydrates in the human body, correlate to distinct functions, necessitating accurate identification. Isomeric structures of carbohydrates are difficult to identify by many methods; however, Raman spectra provide distinct spectra associated with subtle changes in chemical structure. The Raman effect is weak as only 1 out of 10¹3 photons Raman scatter, so surface-enhanced Raman spectroscopy was developed as a way to increase signal in order to collect more chemical specific information. SERS uses metal nanostructures, which are irradiated with a laser at their plasmon resonance frequency, resulting in enhancements of up to 10¹³ in the Raman scattering of the molecules of interest on the surface. Even though this method has advantages over Raman scattering, there are still drawbacks, as nanostructures only interact with molecules that are within a few nanometers of the surface, and it can be difficult to obtain reproducible signals using SERS. Recent work in the Schultz lab has led to the development of a flow cell which uses a sheath flow to force the analyte close to the surface of the nanostructures, leading to increased sensitivity and reproducible signals when working with analytes in solution. Throughout this year, work has been done to show that simple sugars acting as model carbohydrates can be detected using the flow cell, both with a normal SERS substrate and with SERS substrates functionalized using a self-assembled monolayer of decanethiol and mercaptohexanol. The end goal of this project is to identify specific glycans based on their Raman spectrum by using the developed SERS flow detector.

Age impact on Stroop Effect

Maddie Ritchison Triton Elementary School

The Stroop Effect is a test that is an experiment of interference in the reaction time of a task. In this case the task is to say the color of the written word aloud. The Stroop Effect was published by John Ridley Stroop in 1935. This experiment showed me what the difference is in time are for different age groups to correctly recognize the color and state the name of the word. Different tasks take different parts of the brain to process. It takes one part of the brain to be able to state the written word and another part of the brain to be able to recognize the color. When the brain is asked to perform both tasks, this creates conflictive processing. In return, this causes several delays and slows down the reaction time when answering test number 3.In my experiment, I printed three different tests with answer keys. I found 30 volunteers (five males and five females each in three age groups of 10-20, 21-40 and 41-60). Each volunteer took a series of three tests and I recorded the data in my 'sloppy copy' graph. The tests consisted of test number 1 (state the word printed in black ink), test number 2 (state the word printed in a color of ink that was not matching the written word), and test number 3 (recognize the color of the ink). Each test consisted of 50 words and was allowed thirty seconds. My hypothesis for this experiment was the middle aged group, or 21-40, would have the best results. My hypothesis was correct. The results show the overall total of correct words was ages 21-40 group with an average of 30.4 correct words.

Oral Presentation

Distinguishing Sextic Curves Via Syzygies

Austin Rodgers
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Mathematics
Advisor: Claudia Polini, Dept. of Mathematics

The current focus of my original senior thesis research with Professor Polini is centered on the following mathematical problem:

Let C be a rational plane curve of degree 6. We consider the syzygies of the parametric equations defining C. Let (d,t) be the degrees of the generators of the syzygy module. A general curve with (d,t) = (3,3) will have ten double points as singularities. The same is true for a general curve with (d,t) = (2,4). How can we distinguish these two sets of points geometrically? Algebraically the curves are very different, i.e. their Hilbert Burch matrices are a distinguishing feature. A general rational plane curve of degree 6 will have (d,t)=(3,3). However it is still an open question how to geometrically characterize the closed set (given by the curves with (d,t)=(2,4)).

The interest around this problem centers on the interplay between commutative algebra and geometry. The establishment of a dictionary passing from algebra to geometry has been a central aspect of this field since its inception. Solving this problem for the isolated case of projective plane sextics may provide a method by which other classes of singular plane curves can be distinguished geometrically when the naïve approaches fail to give distinct invariants. Practically speaking, we are looking for a geometric invariant that completely characterizes the closed condition of (d,t)=(2,4) on the parameter space for sextic curves.

Temporal Variation of Protozoan Parasites in Singapore Macaque Hosts

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Anthropology and Biological Sciences
Justin Wilcox and Hope Hollocher, Dept. of Biological Sciences
Advisor: Hope Hollocher, Dept. of Biological Sciences

Characterization of parasite communities in wildlife populations is important for managing zoonotic diseases, describing coevolution of parasites and hosts, and understanding parasite-parasite interactions. While parasite populations are of keen interest to ecologists and global health researchers, we still know little about their temporal and spatial variation in realistic, geographically varied, and species-rich environments. Mathematical models have been theorized to predict how parasite populations shift over time in hosts, but such models generally lack empirical verification, focusing specifically on single-host, single-parasite systems. This project studies the level of temporal variability across eight protozoan parasite genera in a structured population of long-tailed macaque monkeys (Macaca fascicularis) on the island of Singapore. Using fecal samples from macaques at several sites collected from 2011 to 2013, parasite presence and shedding data was determined by trichrome-stained microscopy techniques. Several ecologically important genera were discovered, including Cryptosporidium, Cyclospora, Entamoeba, and Endolimax. With this information, multivariant and distance-based statistical analyses were used to determine overall temporal stability and site-dependent variation over the three year period. Preliminary results suggest that, while parasite communities remained fairly consistent in terms of taxonomic richness, prevalence of certain genera varied across years. Additionally, a major outbreak of *Balantidium* coli, a previously rarely detected zoonotic pathogen, was observed in 2012. Our results indicate that wildlife parasite community structure at a singular time point may not be indicative of the long-term patterns that occur in these assemblages. Consequently, parasite survey results from one time point used to generalize to a broader timeframe could be significantly skewed. While species richness may remain stable, specific parasite genera fluctuations can still detrimentally impact individual host health and increase disease transmission. Ultimately, these findings advocate for a cautious approach to extrapolation of enzoic parasite data by researchers and public health organizations. Informed management of zoonosis may require more consistent surveillance strategies that capture year-to-year variation.

Analysis of schematic one-level and two-level nuclear shell models

Jason Saroni College of Science Physics Advisor: Mark Caprio, Dept. of Physics

In the nuclear shell model, nuclei with several nucleons outside closed major shells have a prominent short-range residual interaction which can approximately be accounted for through pairing forces and deformation-inducing quadrupole forces. Here these forces are considered in a valence space of one and two shells. The calculated results are compared to test cases using a nuclear shell model code called the ArbModel. The ultimate goal is to map out the competition between the pairing and quadrupole forces.

A low-cost device to detect amplified DNA for pathogen diagnostics

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Biological Sciences and Theology
Scott Howard, Dept of Electrical Engineering
Sunny Shah and Satyajyoti Senapati, Dept. of Chemical and Biomolecular Engineering
Advisor: Hsueh-Chia Chang, Dept. of Chemical and Biomolecular Engineering

Polymerase Chain Reaction or PCR is one of the most powerful bio detection assays available in research and medicine today due to its ability to amplify a few copies of nucleic acids into millions of copies in a matter of hours. In medicine, PCR can be used to detect specific sequences of nucleic acids in order to diagnosis disease. While PCR is considered as a current gold standard for diagnostics, it has several limitations namely: high cost for instrumentation (>\$10,000), high power requirement (>400W), need for trained personnel and lack of portability. The goal of our research is to develop a low-cost, portable integrated nucleic amplification and detection platform for rapid (<1 hour) detection of nucleic acids from pathogens. A portable, low-power PCR unit to perform nucleic acid amplification has already been developed in the Howard Laboratory (Electrical Engineering). Our research focuses on improving the nucleic detection post amplification. Currently, researchers use the cumbersome gel electrophoresis process to determine if amplification occurred and whether the target nucleic acid was present. This process takes over an hour and requires costly devices and materials. We have developed a microfluidicbased nanomembrane sensor that can replace the gel electrophoresis as the detection platform. The sensor works on the principle that the flow of current through an anion-selective nanomembrane changes upon adsorption of target nucleic acids (RNA or DNA). In the case of a successful PCR reaction, there will be a higher concentration of amplified nucleic acids that will result in an increase in changes in the electrical signal of the sensor whereas an unsuccessful reaction will produce a relatively low change in signal. This difference in the signal changes can be used as an indicator for the presence or absence of target nucleic acids. Preliminary results have shown our ability to calibrate changes in electrical signal based on the number of amplification cycles and our ability to selectively predict the presence of target nucleic acids in a few minutes. This detection combined with the low-cost PCR instrument will realize an integrated amplification-detection device that is low-cost, low-power, accurate and easy-to-use.

Predicting Pitch Outcomes Based on Batter and Pitcher Profiles

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Applied and Computational Mathematics and Statistics
Joseph Germino
Mendoza College of Business
Finance

Advisor: James Delaney, Dept. of Applied and Computational Mathematics and Statistics

In baseball, one of the most common strategic decisions that must be made throughout the game is determining which pitch to throw in which situation. Teams spend millions of dollars each year on scouting reports to determine a specific hitter's weaknesses and strengths and the best approach when facing them at the plate. We aim to develop a computer model that can predict the likelihood of particular outcomes and decrease the necessary spending for such scouting reports. Using PITCHf/x data, we will develop batter and pitcher profiles using statistics, such as handedness, strikeout percentage, homerun percentage, contact percentage, and other measures of plate discipline, and determine how these batters usually perform against pitches with particular movement in a particular location. We will use all of the player profile statistics and pitch profile statistics as inputs in a logistic regression model. The model will then determine the probability of particular outcomes such as strike, ball, contact, and homerun. Our definitions of these outcomes are all-inclusive and mutually exclusive. Once a model is obtained, we hope to optimize the model to find the ideal location to throw a particular pitch in a given situation. A successful model could help in developing future scouting reports for baseball teams.

Developing an Effective Immunotoxin that Targets Cells Overexpressing ErbB2

Luqun Shen College of Science Biological Sciences

Kelsey Weigel, Clayton Thomas, and Lauren Drapalik, Dept. of Biological Sciences Advisors: Shaun Lee, University of Notre Dame, College of Science, Dept. of Biological Sciences and Zachary Schafer, Dept. of Biological Sciences

Approximately 30% of all breast cancers involve the overexpression of ErbB2, which can promote cell proliferation and oppose apoptosis. Currently, the best treatment option for ErbB2-positive breast cancers is the drug Herceptin. But while Herceptin has shown promise, patients are known to eventually develop resistance to the drug, leading to the need to implement alternative methods of treatment. One example of alternative treatments that are being investigated to overcome these shortcomings are immunotoxins. Immunotoxins are composed of a targeting ligand and a toxin, allowing for the selective destruction of cancer cells. Here we attempt to develop an immunotoxin that will specifically target cells overexpressing ErbB2. In addition, because the immunotoxins we are interested in exert their cytotoxic effect at the cell membrane and do not require internalization, cells will have a more challenging time becoming resistant to it. First, cells overexpressing ErbB2 were treated with a variety of peptides derived from bacteriocins and, utilizing an ethidium homodimer assay, cell death was assessed. We determined that the peptide NL11-PSA, composed of an ErbB2 targeting ligand (NL11) and a toxin derived from pardaxin (PSA), showed the strongest toxicity and specificity of all the peptides tested. In addition to screening these peptides, we have attempted to produce NL11-PSA as a toxic and specific recombinant protein. In tandem, these approaches represent a multi-faceted approach to target ErbB2 and our data suggests that NL11-PSA could be used as an effective therapeutic to eliminate ErbB2-positive breast cancer cells.

Effects of APC loss on Wnt/β-catenin Signaling in Pancreatic Cancer

Kaitlyn Simmons College of Science Science Preprofessional Studies

Advisors: Jenifer Prosperi, Indiana University South Bend School of Medicine, Harper Cancer Research Institute, Dept. of Biological Sciences, and Reginald Hill, Harper Cancer Research Institute, Dept. of Biological Sciences

Loss of the Adenomatous Polyposis Coli (APC) tumor suppressor gene in colorectal cancer elicits rapid signaling through the Wnt/β-catenin signaling pathway. In contrast to this well-established role of APC, recent studies from our laboratory have demonstrated that APC functions through Wnt-independent pathways to mediate in vitro and in vivo models of breast tumorigenesis. Pancreatic ductal adenocarcinoma (PDAC) has a five-year survival rate of 5-6% and an overall median survival of less than one year. APC is lost in a subset of pancreatic cancers, but the impact on Wnt signaling or tumor development is unclear. Given the lack of treatment strategies for pancreatic cancer, it is important to understand the functional implications of APC loss in pancreatic cancer cell lines. Therefore, the goal of this project is to study how loss of APC affects Wnt pathway activation and ultimately tumor development. Using lentiviral shRNA, we successfully knocked down APC expression in six pancreatic cancer cell lines (L3.6, Mia Paca, BXPC3, HPAF2, Aspc1, Hs766T). While no changes were observed in localization of β -catenin or expression of Wnt target genes, reporter assays to assess β -catenin/TCF interaction found an increase in TCF reporter activity in one of the Aspc1 knockdown cell lines. Despite this relatively modest activation of the Wnt/β-catenin pathway, the majority of APC knockdown cell lines exhibit an increase in cell proliferation. Future studies will include migration, soft agar and chemotherapeutic response assays. By performing these experiments, we hope to exploit APC loss in pancreatic cancer as a targetable therapeutic mechanism.

Oral Presentation

Network Motif-Inspired Evolution of Hodgkin-Huxley Neuronal Networks with Spike-Timing Dependent Plasticity

Justin Skycak
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Computer Science and Mathematics
Advisor: Dervis Vural, Dept. of Physics

Analysis of statistically significant subgraphs, or network motifs, offers a promising approach to the study of complex networks: if a subgraph occurs much more frequently in a functional network than in a random graph, it might play an important specific role in the network. Network motifs, the "building blocks" of complex networks, are especially advantageous tools for understanding dynamic networks (e.g. brain neuronal networks) because network motifs must be must be stable under normal network inputs. Using a Hodgkin-Huxley computational model with spike-timing dependent plasticity (STDP), we will evolve A) all possible nontrivial neuronal connectivity configurations for 1, 2, 3, and 4 neurons, and B) specific neuron cycles for 2, 3, 4, and larger numbers of neurons, under periodic step pulses at various frequencies. We will identify rules that govern how the configurations evolve to stable configurations, which are potential network motifs, and we will use these rules to evolve random networks. Lastly, we will compare our results to those obtained by evolving the same random networks under Hodgkin-Huxley dynamics with STDP learning.

Quantification of Side Reactions in SCVcP of A-BIEM and MMA Hyperbranched Polymer

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Chemistry and English
Robert Graff and Xiaofeng Wang, Dept. of Chemistry and Biochemistry
Advisor: Haifeng Gao, Dept. of Chemistry and Biochemistry

Traditionally, hyperbranched polymers can be synthesized with a facile one-pot self-condensing vinyl copolymerization (SCVcP), a sharp contrast to the multi-step synthesis of dendrimers, the structural analogs of hyperbranched polymers. However, the hyperbranched polymers synthesized in the one-pot reaction suffer from poorly defined structure, high polydispersities, and are difficult to characterize due to inevitable side reactions. Therefore, quantifying these side reactions can make polymer characterization easier and improve the utility of hyperbranched polymerization. In this project, 2-(1-(2-((2-bromo-2-methylpropanoyl)oxy) ethoxy)ethoxy)ethyl methacrylate (A-BIEM) inimer and methyl methacrylate (MMA) were copolymerized to synthesize a degradable hyperbranched polymer. The reaction kinetics were monitored with samples being taken at intervals of about 25%, 50%, 75%, 99% conversion. The samples were then degraded and the fragments were analyzed by size exclusion chromatography to identify and quantify the side reactions, more specifically radical-radical coupling, occurring in the reaction with increased conversion.

Gao, C.; Yan, D. Hyperbranched Polymers: from synthesis to applications. Prog. Polym. Sci. 2004, 29, 183-275.

Oral Presentation

Environmental DNA detection of the invasive red-eared slider turtle (Trachemys scripta elegans)

Michael Spear College of Science Environmental Sciences

Advisors: Crysta Gantz, Mark Renshaw, and David Lodge, Dept. of Biological Sciences

Invasive species cost the United States economy an estimated \$137 billion annually, with nearly \$6 billion of that due to aquatic invaders of the Great Lakes region. One of those invaders, the red-eared slider turtle (RES) (Trachemys scripta elegans), causes ecological damages around the world as it is introduced to non-native habitats through the global pet trade. An emerging management tool for aquatic invaders like the RES is surveillance using environmental DNA (eDNA) detection. Using bioinformatics software, we designed species-specific primers to isolate RES DNA from the environment, choosing those primers from a section of the Cytochrome B gene of the RES's mitochondrial genome. Sampling from aquaria in local pet stores, nature centers, and zoos, we chloroform-extracted DNA from the habitats of RES and non-target species to ensure a robust quantitative PCR (qPCR) assay that only amplified RES DNA. Once a reliable assay was established, we examined samples from sites of known historical RES occurrences in Chicago and Northern Indiana. Comparing amplification results to known standards of RES DNA concentrations, the qPCR technique allowed us to determine both presence and DNA copy number. To date, our assay has consistently amplified RES DNA from aquaria with known RES presence, but has not amplified DNA from non-target species samples, indicating a stringent and successful protocol. Field samples from water bodies of known historical RES occurrences but unknown current occupancy state have resulted in no positive detections, indicating the probable absence of RES at these sites. These results are encouraging, as they indicate that RES have likely not permanently established at the sites of historical occurrence. We recommend more comprehensive sampling of the Great Lakes region to better understand the true distribution of this dangerous invasive species.

A generalized framework for nucleosynthesis calculations

Trevor Sprouse
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Physics
Ani Aprahamian and Matthew Mumpower, Dept. of Physics
Advisor: Ani Aprahamian, Dept. of Physics

Simulating astrophysical events is a difficult process, requiring a detailed pairing of knowledge from both astrophysics and nuclear physics. Astrophysics guides the thermodynamic evolution of an astrophysical event. We present a nucleosynthesis framework written in Fortran that combines as inputs a thermodynamic evolution and nuclear data to time evolve the abundances of nuclear species. Through our coding practices, we have emphasized the applicability of our framework to any astrophysical event, including those involving nuclear fission. Because these calculations are often very complicated, our framework dynamically optimizes itself based on the conditions at each time step in order to greatly minimize total computation time. To highlight the power of this new approach, we demonstrate the use of our framework to simulate both Big Bang nucleosynthesis and r-process nucleosynthesis with speeds competitive with current solutions dedicated to either process alone.

Manual annotation of G Protein-Coupled Receptors (GPCRs) in the genomes of Lutzomyia longipalpis and Phlebotomus papatasi

Samuel Tadros
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Biological Sciences
Gloria Giraldo-Calderon, Dept. of Biological Sciences
Advisor: Mary Ann McDowell, Dept. of Biological Sciences

Sequencing the genomes of *Phlebotomus papatasi* and *Lutzomvia longipalpis* will help in the task to combat sand fly-borne diseases such as leishmanaisis, a parasitic disease transmitted through these vectors. These sequences will provide valuable resources for improving control or eradication strategies to stop the transmission of these diseases. One such strategy is the use of G protein-coupled receptors (GPCRs) as new targets for insecticide chemistries. GPCRs play roles many essential insect pathways and can be specifically targeted with small molecules, making GPCRs good insecticide targets. We used bioinformatic approaches to identify GPCRs in the genomes of these two sand flies. A new classifier pipeline was created to identify the GPCRs from the P. papatasi and L. longipalpis genome assemblies at the database VectorBase using a the set of known GPCR peptides from Aedes aegypti, Anopheles gambiae, Apis mellifera, Drosophila melanogaster, Homo sapiens, and Pediculus humanus. The identified sand fly GPCR sequences were aligned using BLAST against the non-redundant protein sequences in NCBI. Putative functions were assigned based on the best and the most informative BLAST hits, in most of the cases the later was from D. melanogaster. The sand fly sequences were aligned with homologous genes, mostly from insects used in the classifier pipeline, using MultAlin. The sand fly gene models were manually corrected using the annotation tool Artemis. Identified and manually annotated GPCRs were used to search (tBLASTn) the sandflies genome scaffolds for additional GPCR genes. When available, the gene models were confirmed using transcript evidence from Expressed Sequence Tags (ESTs) and RNA sequencing (RNAseq). In total, 94 GPCRs from P. papatasi and 92 from L. longipalpis were annotated and submitted to VectorBase. These gene models were the first GPCRs from these two species to be throughly annotated, and they will assist in the development of novel insecticides.

Synthesis of N-glycosylated Cetuximab in Bombyx mori

Denise Tarnowski College of Science Advisor: Malcolm Fraser, Dept. of Biological Sciences

As more knowledge is gathered on a genetic and molecular level, the demand for recombinant proteins is rising in both research and therapeutics. Many human proteins that have biomedical significance are glycoproteins, such as antibodies and cytokines. N-linked glycosylation is the most common type of glycosylation with 90% of all glycoproteins being N-glycosylated. Current systems used for recombinant protein synthesis cannot produce higher eukaryote glycoproteins with the correct carbohydrate side chains at greater than 30 to 40% of the total product composition. Differences in glycosylation can cause an immunogenic response making the proteins unfit for clinical use. Thus, it is important to find a system that cannot only create recombinant proteins in a time and cost effective manner, but can also correctly glycosylate those proteins. The silkworm, Bobyx mori, has been proposed and tested as a potential system because it can synthesize and secrete large amounts of protein in its silk glands making it ideal for the mass production of recombinant proteins. We hypothesize that human N-glycosylated proteins can be synthesized with greater homogeneity for the preferred product and easily recovered from silkworm cocoons. A plasmid containing anti-EGFR (Cetuximab) was constructed and microinjected into silkworm eggs utilizing the piggyBac transposon for transformation. The plasmid was first injected into a control parental line and then crossed into the GG1 line that was genetically engineered to include mammalian Nglycosylation enzymes N-acetylglucosaminyl-transferase II (Gn-TII) and galactosyltransferase (Gal-T). Fluorescent eye markers have indicated that the plasmid is expressed in the silkworms. A SDS-PAGE gel and western blot were run to confirm the presence of the antibody in the cocoons. An ELISA was used to assess the binding affinity of the antibody to its substrate and the most effective extraction protocol. Further work is being done to increase protein yield and determine the molecular structure of the glycans present on the antibody.

Autophagy and Dengue Fever transmission

Madeleine van Zuylen College of Science Biochemistry

Advisors: Matthew Eng and David Severson, Dept. of Biological Sciences

Dengue Fever is a major worldwide health concern that impacts the lives of millions of people. The Dengue virus (DENV) infects a host mosquito (*Aedes aegypti*) and is then transmitted to humans. DENV is aided in replication and transmission to humans by autophagy in mosquito mid-gut cells. This project uses DAPI and LysoTracker staining methods and microscopy to indicate autophagy in fat body and midgut tissue in *Aedes aegypti* after various manipulations to the autophagy gene.

Topological Methods in Data Analysis

Jonathan Vandenburgh College of Science Mathematics

Advisor: Mark Behrens, Dept. of Mathematics

With the increasing size and complexity of data sets, there is a need for new methods of data analysis. In the past few decades, researchers have begun applying topology, the mathematical study of shape, to data analysis. Topological data analysis relies on the mathematics of persistent homology to understand the homology groups of a complex associated to a data set. This mathematical analysis gives insight into the shape of the data set and allows one to visualize high dimensional data in lower dimensions. I will discuss these methods of applied topology, including how to form a complex and how to compute the homology groups. I will give an overview of some applications of topological data analysis, including applications to data sets related to breast cancer, diabetes, and basketball. I will conclude with some possible future theoretical and practical developments in topological data analysis.

Novel Interactions in the Gephyronic Acid Biosynthetic Pathway and Production of Gephyronic Acid
Analogs from Advanced Synthetic Substrates

Meredith Vieira College of Science Biochemistry

D. Cole Stevens and Matthew Wilson, Dept. of Chemistry and Biochemistry Advisor: Richard Taylor, Dept. of Chemistry and Biochemistry

Our lab is interested in the pharmacophoric link between the myriaporones, tedanolides, and gephyronic acid. These structurally similar but geographically distinct natural products are potent eukaryotic protein synthesis inhibitors. Our lab has put significant effort into the syntheses, structural assignments, and biological investigations of the myriaporones and gephyronic acid. Additional biological study of these molecules is limited by poor synthetic and biological access. To address this issue, we developed a heterologous platform for the production of linear polyketide homologs in engineered strains of Escherichia coli from advanced synthetic substrates. Initial trials of this platform successfully produced novel analogs of gephyronic acid from an advanced synthetic substrate. These studies revealed a significant revision in the currently accepted biosynthesis of gephyronic acid, suggesting a previously unreported protein-protein interaction involved in polyketide synthesis. Additional experiments to confirm the existence of this interaction and understand its nature are ongoing. These experiments will also produce additional novel analogs of gephyronic acid. With these results, we hope to elucidate the gephyronic acid biosynthetic pathway in order to produce gephyronic acid-myriaporone hybrids and novel analogs, which will allow us to study the pharmacophoric relationship between the two classes of molecules.

Oral Presentation

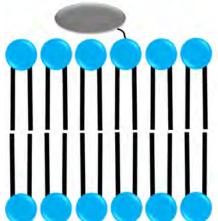
pH-responsive fluorescent probe for anionic phospholipid sensing at the membrane surface

Katelyn Virga
College of Science
Chemistry
Kasey Clear, Dept. of Chemistry and Biochemistry
Lawrence Gray
College of Science
Chemistry

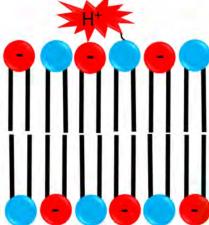
Advisor: Bradley Smith, Dept. of Chemistry and Biochemistry

Surface charge on biological membranes is known to play an important role in processes such as membrane fusion and recruitment and binding of peripheral proteins. Regulation of surface charge typically occurs by changes in the expression of anionic phospholipids. Fluorescent probes are being explored as a new method of detecting changes in membrane surface charge due to the presence of anionic phospholipids. One design involved a pH-responsive pentamethine cyanine dye (Cy-5) conjugated to a phosphatidylethanolamine lipid. The probe exhibited ratiometric absorbance and "turn on" fluorescence in presence of phosphatidylserine (PS) and other anionic phospholipids. As the concentration of PS increased from 0%-50% the pKa of the probe increased by approximately 1 unit, and the fluorescence from the "on" state increased in intensity. A possible explanation for this observation is an ionic attraction between the positively charged dye and the anionic phosphatidyl serine at the membrane surface. The project is also examining other probes with different linkers to determine if there is an effect on the magnitude of the pKa shift.

Neutral Membrane Deprotonated "Off" State Favored



Anionic Membrane Protonated "On" State Stabilized



Climate Change's Effect on Montana's Bunchgrass Prairie

Zoe Volenec College of Science Economics and Environmental Sciences Advisor: Gary Belovsky, Dept. of Biological Sciences

Plants form the foundation for all terrestrial food webs, thus shifts in their phenology and productivity have the potential to alter ecosystem functions and drive bottom-up community effects. One driver of these shifts is climate change, exemplified by altered temperature and precipitation regimes. Over the past 35 years at the National Bison Range, temperature has increased by 0.6°C, while precipitation has decreased by 26%, but increased in the plants' May-June growing season. IPCC models predict future increases in temperature that could affect the prairie's ability to sequester carbon and ultimately impact the biodiversity present in this endangered ecosystem. The objective of this project is to predict the various effects that elements of climate change, such as increased temperature and changes in precipitation levels and seasonality, will have on bunchgrass prairie production and species composition at Montana's National Bison Range. Using a two-year multi-factor experimental setup, a passive nighttime warming system was implemented, along with a 20% increase in precipitation applied on a seasonal and summer-long timetable. The ecosystem impacts were measured through changes in soil moisture, inorganic and organic nitrogen levels, net primary productivity (NPP), and plant species composition in the experimental plots. After the first year of the study, results indicate that the treatments had the intended effect with significant temperature increases with exposure to passive warming (p=0.00004) and significant soil moisture increases in plots receiving increased precipitation levels (p=0.002). The radiometer data of the first field season revealed that precipitation treatments were already having an effect on NPP, as average biomass produced over the course of the summer was significantly higher in plots receiving a moisture treatment (p=0.045). Analysis of nitrogen samples is still underway, but alterations in nutrient cycling, as well as plant die-off rate and vegetation composition will likely appear after the second year of experimentation.

Combined genetic control of cell body degeneration and axon growth in Drosophila photoreceptors

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Advisor: Joseph O'Tousa, Dept. of Biological Sciences

Axons, the signal-conducting processes of neurons, are fragile and can be lost due to injury or neurodegenerative disease. Emerging evidence suggests the presence of highly conserved neuronal regulatory systems responsible for simultaneously dismantling dendritic arbors and regrowing axons in injured neurons. In one such pathway, the subject of our research, the signaling protein Wallenda (Wnd) conveys information on axonal injury to the neuronal nucleus. Wnd then coordinates an appropriate response to injury through the downstream protein kinases Hemipterous (Hep) and Basket (Bsk) and through the transcription factors Fos and Knot. We developed the model system of photoreceptor cells in the retina of the fruit fly Drosophila melanogaster to study this process. We show that Wnd activation is sufficient to induce loss of the light-detecting protein Rhodopsin (Rh1) in the photoreceptor cell body and to generate proliferative axon growth at synaptic terminals. These effects are removed with ectopic overexpression of Knot or knockdown of Hep or Fos, suggesting that the conserved signaling pathway is operational within photoreceptors. We will use the photoreceptor system to define the vet-unknown specific players of the transcriptional program activated by the Wnd pathway. This aim which will clarify the mechanisms by which Wnd and its effectors bring about the phenotypes of Rh1 loss and axon growth. Because the Wnd pathway is evolutionarily conserved, this research will illumine efforts to understand axonal degeneration in humans as well. Further knowledge of the Wnd pathway's parameters and effects will therefore potentially impact therapeutic approaches to prevent axon loss in neural injury and neurodegenerative disease.

Carbon-14 Graphitization Chemistry

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Physics
Advisor: Philippe Collon, Dept. of Physics

Accelerator Mass Spectrometry (AMS) is a process that allows us to analyze the mass of materials. It is a powerful process because it can separate rare isotopes with very low abundances from large backgrounds. Essentially it is the perfect toll for finding a "needle in a haystack." Another advantage of AMS is that it only requires small amounts of sample material for measurements. An important application of this process is radiocarbon dating because it allows rare 14C isotopes, which have a half-life of t1/2 = 5730years, to be separated from the stable 14N background which is 10 to 13 orders of magnitude larger. Furthermore, only small amounts of the old and fragile organic sample material are necessary for such a measurement. Our group focuses on this radiocarbon dating through AMS. When performing AMS, the sample needs to be loaded into a cathode at the back of an ion source in order to produce a beam from the material to be analyzed. For carbon samples, the material must first be converted into graphite in order to be loaded into the cathode. The undergraduate AMS group is responsible for the conversion of the organic substances into graphite. In order to graphitize the samples, a sample is first combusted to form carbon dioxide gas and then purified and reduced into the graphite form. So far, the group has constructed an apparatus to perform this graphitization, gone through several trial runs to work through and improve the process, and successfully graphitized several samples. The next step in the process will be to take AMS measurements with the samples.

Social status and parasitism in male and female vertebrates: A meta-analysis

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Parasites can induce costs that negatively impact infected individuals by limiting daily activity, reducing fitness and causing mortality. In humans, it is generally understood that there is an inverse correlation between parasite load and socioeconomic status. However, the relationship between parasite load and social status in nonhuman vertebrates is much less understood. The type of dominance hierarchy (i.e. linear, nepotistic, age-based) an individual lives in might explain variation in parasitism between dominant and subordinate individuals. In this meta-analytic review, we investigated status-based variation in parasitism by evaluating four different frameworks: the priority of access model, the trade-offs model, the stress response model, and the allostatic load model. A comprehensive literature review yielded over 20 scientific studies across 15 taxa. Our preliminary findings indicate that dominant males tend to have higher rates of parasitism than subordinate males. While there have been a multitude of studies assessing the association between social status and parasitism in males, there have been very few studies of females. Our study of the correlation between social status and parasitism for female vertebrates is still under investigation. We report our findings using an allostatic load framework, which proposes that an individual with high allostatic load will exhibit decreased immune function, potentially leading to increased rates of parasitism.

The Effect of Different Products on Moisture Retention

Amy Wyse ETHOS Academy

It is crucial for horse owners to have their arena footing in the right condition, not too dusty and dry, but not too wet. Sadly, it is difficult to maintain arenas so meticulously because horse owners often do not have the time to water them when needed. This prompted the question What additive works to best retain moisture in horse arena footing? Ten trials were conducted. These trials each had five different tests, each with a different additive. Test A had no additive, Test B had tapioca, Test C had pine shavings, Test D had calcium chloride, and Test E had Soil Moist. Each test contained two cups of arena footing, two tablespoons of the additive, and three tablespoons of water. At the beginning of the eight days for testing the tests were weighed, and they were weighed again at the end. The hypothesis was that the calcium chloride test would retain the most moisture because of its hydroscopy and deliquescence. The independent variable was the additive. The dependent variable was the percent of weight (moisture) retained, and the control was the test with no additive. The hypothesis proved correct as calcium chloride retained 96.6901%. Then the Soil Moist retained 92.1468%, and the tapioca retained 91.4145%. The pine shavings retained 90.6522%, and the no additive retained the least with 90.6277%. It was observed that the calcium chloride made the arena footing very slippery and that the Soil Moist made it fluffy, which is good for arenas.

Oral Presentation

Counting Elliptic Curves with Prescribed Torsion

Xiao Xiao College of Arts & Letters Mathematics and Philosophy Advisor: Andrei Jorza, Dept. of Mathematics

The Mordell-Weil theorem states that the group of rational points on an elliptic curve E over the rational numbers is a finitely generated Abelian group. A theorem of Mazur says that the torsion subgroup of E(Q) must be isomorphic to one of 15 groups. It is natural to ask how often each of these 15 groups occurs. This presentation gives an answer to this question. For any E/Q given in a minimal equation of the form $y^2=x^3+Ax+B$ and a prescribed torsion subgroup, we also give a complete Diophantine conditions on the coefficients A and B for E(Q) to contain a subgroup of that form.

Volatility Estimation and Applications in Stock Options Trading Decisions

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Advisor: Huy Huynh, Dept. of Applied and Computational Mathematics and Statistics

Volatility is essential in determining the option prices. Currently there are several estimators that are used to estimate historical volatility. In particular, Parkinson estimator and Yang-Zhang estimator are among the most popular ones. In this study, we pick stocks which have weekly options from the stock pool of NASDAQ 100 Index, divide the historical prices of these stocks into short-term periods (seven days), and calculate the estimated volatilities using Parkinson estimator and Yang-Zhang estimator. We predict the volatilities of the following seven days with a simple AR model suggested by [Jacob and Vipul, 2008]. We compare the predicted volatilities to the implied volatility and find the profits of different trading strategies based on Parkinson and Yang-Zhang estimators. Finally, we compare the performance of the two estimators based on the profits obtained from these strategies.

The Role of the mirn23a MicroRNA Cluster in Hematopoiesis and B-Cell Acute Lymphoblastic Leukemia

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Biological Sciences
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Previously our laboratory has shown that the miR-23a miRNA cluster (mirn23) promotes granulocyte/macrophage myeloid development at the expense of B-cells (lymphoid) in overexpression studies. Consistent with this phenotype we have observed that mice lacking the mirn23a gene have increased lymphoid (adaptive immune cells) and decreased myeloid (innate immune cells) progenitors in the bone marrow. To investigate potential pathways regulated by mirn23a that inhibit B-cell differentiation, we looked at lymphoid gene expression networks in B-cell lines overexpressing mirn23a. Gene expression and western blot analysis showed that mirn23a decreased expression of B-cell specific transcription factors Ebf1 and Pax5. Since these factors are not known to be direct targets of mirn23a, we looked at known mirn23a target Trib3 as a potential mechanism to regulate Ebf1 and Pax5 through Akt and FoxO1 signaling. Overexpression of mirn23a caused decreased Trib3 gene expression and western blot analysis showed FoxO1 protein also decreased. In acute lymphoblastic leukemia, Ebf1 and Pax5 are tumor suppressors and Akt1 is oncogenic. Mirn23a's ability to downregulate Ebf1 and Pax5, as well as increase Akt activity, is suggestive that it plays a role in the development of lymphoid leukemia. Gene expression array analysis shows that mirn23a miRNAs are overexpressed in MLL-AF4+ and Bcr-Abl+ ALL (acute lymphoid leukemia) cells. Studies are currently underway using mirn23a-/- mice to determine if mirn23 miRNAs contribute to the development of ALL in transplantation models of Bcr-Abl-induced leukemia. Thus, our data supports the conclusion that mirn23a drives hematopoietic differentiation through the Akt/FoxO1 signaling pathway. This has implications for leukemia development, as mirn23a has the ability to downregulate critical ALL tumor suppressors and activate the ALL oncogene Akt.

Production and biological evaluation of the polyketide naphthocyclinone from the bacteria Streptomyces arenae

Emily Zion College of Science Biochemistry

Advisor: Richard Taylor, Dept. of Chemistry and Biochemistry

Natural products have been valued for their medicinal qualities for thousands of years and have helped to form the basis of modern medicine. The term natural product is used to encompass a wide range of compounds that are derived from natural sources such as bacteria and plants. The polyketide class of natural products includes many diverse secondary metabolites produced by organisms for a survival advantage. Naphthocyclinone, one natural product produced by the bacteria Streptomyces arenae, is a type II, aromatic polyketide that possesses antibacterial properties. In particular, naphthocyclinone belongs to the isochromane quinone family of antibiotics, which also includes the natural products granaticin and kalafungin. The full therapeutic potential of naphthocyclinone, however, is not completely understood. In order to delve deeper into this potential drug source, we plan to extract naphthocyclinone from Streptomyces arenae and complete a full chemical characterization. Efforts will be placed into increasing the production of the natural product through the engineering of the growth media. Another aspect of this project will focus on identifying analogues of naphthocyclinone produced by S. arenae under different growth conditions. Further research will go into investigating the therapeutic properties or other medical functions of naphthocyclinone and its analogues. This investigation of naphthocyclinone could lead to potentially beneficial uses for the natural product, and will contribute to the field of research of natural products and specifically the study of polyketides.