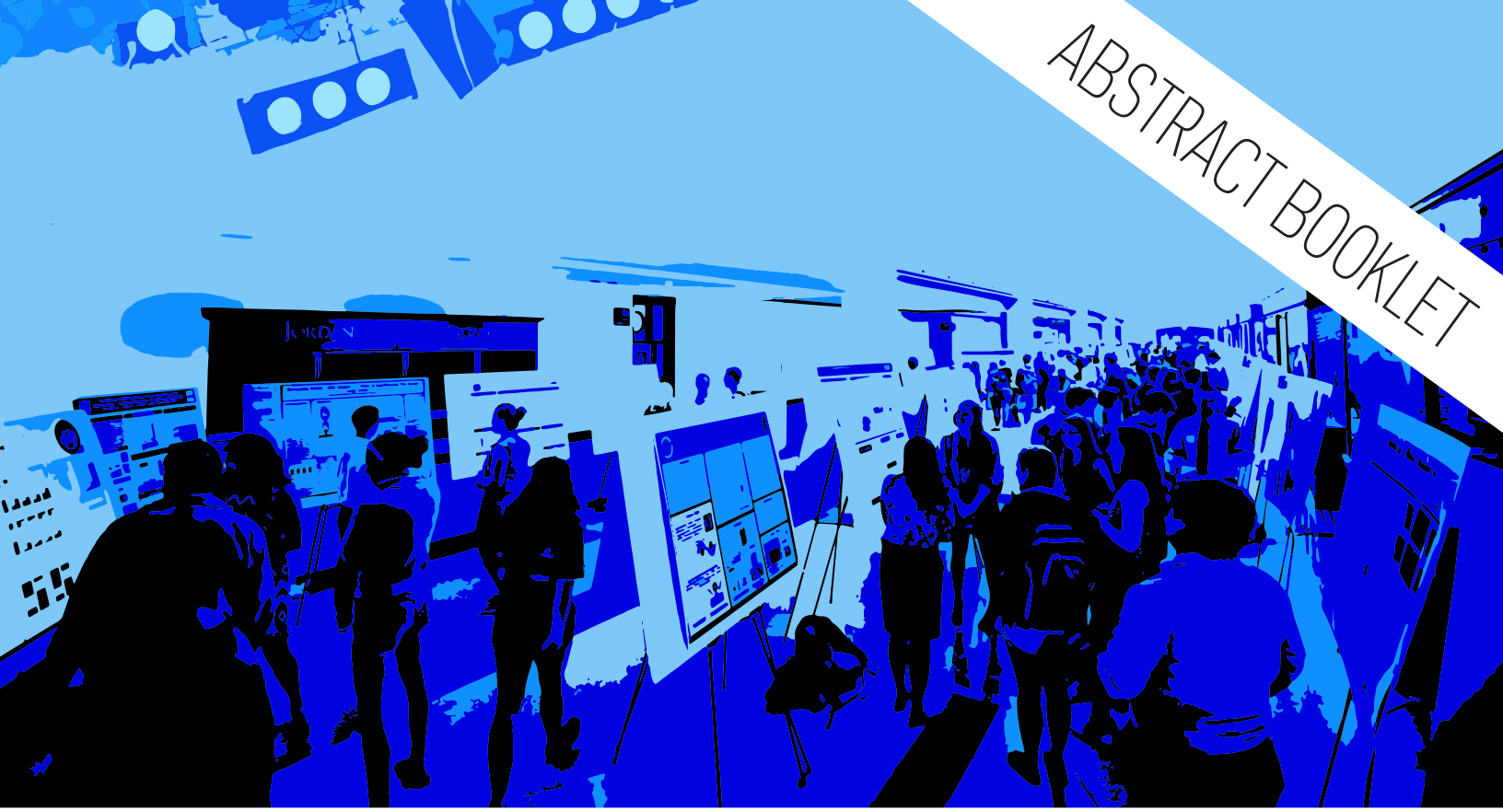

ABSTRACT BOOKLET

COS JAM 2019

COLLEGE OF SCIENCE JOINT ANNUAL MEETING

FRIDAY MAY 5 · 1-5 PM · JORDAN HALL GALLERIA

1:00-1:45	POSTER SESSION I (ODD NUMBERS) SPIRIT OF SCIENCE PRESENTATIONS
1:45-3:00	ORAL PRESENTATIONS I
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2:15	Investigating the Associations Between the Prokaryotic and Eukaryotic Gut Microbiomes in Long-tailed Macaques (*Macaca fascicularis*) **Bailee Egan**
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ARAKI, STEPHANIE (1)

Community-Level Adaptation using Biofilms as an Ideal Study System

Stephanie Araki, Bernard Aulino, David Molik, Katherine Barrett

Advisor: Gary Belovsky, Dept. of Biological Sciences, University of Notre Dame

Microbialites are carbonate structures that contain abundant biofilm communities of bacteria, algae, and Archaea. They are common in shallow saline lakes, where they constitute an important source of benthic primary production and play a critical role in nutrient cycling. The fourth-largest hypersaline (salinity > 5%) lake in the world, the Great Salt Lake (GSL) in Utah contains the world's largest distribution of microbialites, which are an important food source for invertebrates in the lake. Like other saline lakes, GSL receives limited freshwater inflows and has no outlet, which makes it sensitive to changes in precipitation and temperature, which lead to changes in salinity. Despite their importance in the GSL food web, little is known about their response to climate change-induced stresses, such as rising temperature and salinity. To accurately predict how biofilm community composition and aquatic ecosystem functioning will be affected, we focused on the adaptation of these microbialite biofilms to ecologically-relevant stressors. We cultured GSL microbialite biofilms on clay tiles (N=36) at control conditions of 20 oC and 120 ppt salinity for 6 weeks and then randomly assigned tiles to varying combinations of four salinities (90, 120, 150, & 180 ppt) and three temperatures (10, 20, & 30 oC). After four weeks, we performed cell counts to analyze changes in biofilm community composition, and quantified chlorophyll α after four and seven weeks as a measure of primary production. Additionally, after seven weeks, we extracted DNA from all biofilms for sequencing to identify shifts in bacterial and algae community composition across the temperature and salinity treatments. Our preliminary data indicate that biofilms grew best (based on chlorophyll α concentrations) at the highest temperature (30 oC) and at median salinities (120 ppt and 150 ppt), suggesting that GSL microbialites are robust and can grow under stressful conditions.

ASTARITA, EMILY (2)

Paclitaxel Effects on G2/M Arrest in *APC* Knockdown Cells Through Checkpoint Protein Analysis

Advisor: Jenifer Prosperi, Dept. of Biological Sciences, University of Notre Dame

Adenomatous Polyposis Coli (APC) is a tumor suppressor that is mutated or hypermethylated in approximately 70% of sporadic breast tumors with an inclination towards triple negative breast cancer (TNBC). Patients with TNBC often experience chemotherapeutic resistance when treated with traditional chemotherapy, such as paclitaxel (PTX). While PTX acts by stabilizing microtubules, APC is also involved in regulating microtubule stability through mechanisms that are not fully understood. These uninvestigated roles suggest *APC* gene expression may impact the efficacy of PTX in breast cancer treatment. We previously created APC knockdown cells (APC^{KD}) using the TNBC human breast cancer cell line, MDA-MB-157, and determined that APC loss-of-function significantly increases resistance to PTX. We hypothesized that varying microtubule stability in normal versus APC^{KD} cells may lead to a difference in cell cycle protein modulators during G2/M transition. Therefore, we profiled G2/M transition proteins Cyclin B1 and CDK1, including inhibitory and activating phosphorylation sites on CDK1. Western blot analysis indicated that APC^{KD} cells have an increase in total CDK1 expression, with no changes in phosphorylated CDK1 or Cyclin B1 expression. Given that the complex of Cyclin B1 and CDK1 is only active when located in the nucleus, we examined the localization of these cell cycle proteins and found that in untreated cells, CDK1 is preferentially localized to the cytoplasm. Further investigation is required to determine cellular localization after PTX treatment. As CDK1 is up-regulated in the APC^{KD} PTX resistant cells, we asked whether a CDK1 inhibitor, RO-3306, would sensitize the APC^{KD} cells to PTX treatment. Pilot studies have shown that PTX resistant APC^{KD} cells are more sensitive (IC50 = 25.5uM) to RO-3306 compared the parental control (IC50 = 78uM). Combined, examination of these cell cycle protein modulators can further our understanding of PTX resistance in APC^{KD} cells and help to identify a potential therapeutic target.

AUBOURG, MATTHEW/ TIARA, LEILANI (3)

Vector Species and Factors Relating to Malaria Transmission in the DRC

Advisor: Neil Lobo, Dept. of Biological Sciences, University of Notre Dame

Malaria is a mosquito-borne disease and public health problem causing 750,000 deaths annually. Anopheles funestus s.l. and An. gambiae s.l. are primary vectors of human malaria in Africa. Long-lasting insecticide nets and indoor residual spraying have been used as interventions to reduce malaria transmission in the Democratic Republic of Congo (DRC). However, the success of vector interventions is dependent on their overlap with susceptible mosquito behaviors. The goal of this project is to examine site specific vector species diversity and behaviors using house construction as a significant predictor of these factors, through analysis and comparison of mosquito collections in Lodja and Mikalayi, DRC.

Mosquito samples were acquired by human landing capture, from which DNA was isolated, amplified by PCR, and visualized by gel electrophoresis for species determination. Data were analyzed to determine biting location and frequency of a species within a certain type of house at each site. In Lodja, four different vector species were found in houses made of clay, whereas five different species types were found in houses of more durable materials such as concrete. There was a high density of An. coluzzi across all house types. In Mikalayi, species types and densities differed - there were little to no An. coluzzi, but a significant amount of An. moucheti.

Morphological misidentification described contributed to gaps in understanding, further demonstrating the need to discern species-specifc behavior. In Mikalayi, for example, the total misidentification rate is 30.8%, largely due to high rates of A. moucheti misidentification (100%).

BALES, CAYLA (4)

Investigation of the Anti-amyloidogenic Activity of Gastrokine 1

Advisor: David Boone, Dept. of Biological Sciences, University of Notre Dame

Gastrokine 1 (Gkn1) is an 18 kDa protein produced and secreted into the lumen of the stomach. It is stable and protease-resistant, which allows it to resist degradation in the gastrointestinal (GI) tract. To examine the function of Gkn1 in vivo, $Gkn1^{-/-}$ mice were previously generated. $Gkn1^{-/-}$ mice are healthy and have a normal lifespan. However, $Gkn1^{-/-}$ mice have markedly reduced body fat compared to wild type (WT) littermates, and they are resistant to weight gain on a high fat diet. $Gkn1^{-/-}$ mice are not diabetic, have normal appetite and physical activity, and do not malabsorb calories. We hypothesize that Gkn1 influences phenotype through regulation of the intestinal microbiota. Gkn1 prevents a fundamental amyloid function of bacteria, namely biofilm formation. This study investigates the biochemical features of Gkn1 that mediate its anti-amyloidogenic effects, in particular its BRICHOS domain, which is associated with amyloid fiber binding. For in vitro experimentation, a *Kluyveromyces lactis* yeast model was created for generation of large quantities of Gkn1. Site-directed mutagenesis was then used to change specific conserved amino acids in the BRICHOS domain for subsequent generation of mutant protein. To compare the abilities of Gkn1 and mutant Gkn1 to inhibit biofilm formation, biofilm assays were performed with bacterial strain LF82. Preliminary results suggest that certain amino acids in the BRICHOS domain, while conserved in evolution, are not critical for the anti-amyloidogenic activity of Gkn1. We are currently testing other mutant forms of Gkn1 to further elucidate the biochemistry of this function.

BELANS, RACHEL/GILLEN, JOSHUA/ HAGEDORN, KERRY (5)

Using transposon screen to identify novel genes involved in the regulation of virulence in *Mycobacterium marinum*

Rachel Belans, Joshua Gillen, Kerry Hagedorn

Advisor: Patricia Champion, Dept. of Biological Sciences, University of Notre Dame

The ESX-1 secretion system is essential to *Mycobacterium tuberculosis* virulence and utilizes the WhiB6 transcription factor to regulate a feedback loop controlling the expression of secreted virulence substrates. When one of the core components of the ESX-1 membrane complex is missing, such as EccCb1, expression of WhiB6 decreases and the levels of ESX-1 substrates are reduced to avoid accumulation of the substrates in the absence of the secretion system. The molecular pathways connecting the ESX-1 membrane complex in the cytoplasmic membrane and the regulation of gene expression are unknown. We used the model system *Mycobacterium marinum* to conduct a transposon screen in the *ΔeccCb1/whiB6::lacz + pM272b* strain. The *lacZ* reporter in place of the *whiB6* gene signals when the transposon inserts into a gene involved in regulating this feedback loop; we hypothesize that disruption of genes required for sensing and responding to the ESX-1 system will result in reduced levels of *lacZ* expression. When the transposon has been determined to have interrupted a gene involved in *whiB6* regulation, its location within the *M. marinum* genome is isolated and identified to determine which gene is involved in the regulation of WhiB6 expression levels. Using this system, we have identified several novel genes that are involved in the feedback loop regulating the virulence of *M. marinum* including *MMAR_3823*, *MMAR_1630*, and *MMAR_5476*. These genes will be knocked out and characterized in order to elucidate their role in sensing the ESX-1 membrane complex and responding by changing the expression of the *whiB6* gene

BOCKHOLT, KATE/ DIEJOMOAH, MIKE (6)

A Comparison of Diagnostic Content of WebMD and PatientsLikeMe Web Platforms

Kate Bockholt, Mike Diejomaoh, Geoffrey H. Siwo

Many patients use the internet as a resource to not only diagnose themselves but also to treat themselves. The internet is a wonderful resource for many things, but cannot be used without a doctor's diagnosis, especially with the resources currently available, as none of them are reliable enough to be trusted with one's health. In this research project, we looked into listed symptoms at two of the top medical websites used for patient information and empowerment, WebMD and PatientsLikeMe. We cross-checked the symptoms listed for 67 of the top-listed diseases among different categories and found a vast difference in the symptoms listed, mostly in the fact that the same five emotional symptoms are listed across several diseases, while WebMD has diagnosis-based and physical symptoms. We used the data to infer connections among various diseases based on the symptoms provided on both web platforms and to exemplify the drawbacks of self-diagnosis and treatment based on information from these web platforms. We assessed the effectiveness of these platforms especially on the specificity of disease symptoms they provide to aid self-diagnosis and treatment. Essentially, we focused on how these websites may misinform patients and how they could be improved to increase ease of access and give more helpful information to patients. We anticipate this could decrease the instances of unnecessary worry and increasing the extent to which a patient may feel empowered and in control of his or her own treatment. In conclusion, our results could inform a movement toward better patient informational platforms that combine elements of various web platforms such as WebMD and PatientsLikeMe to provide more medically accurate information to patients.

CAHIR, CLARE (7)

Genetic Analysis of ESX-1 Substrates in *Mycobacteria marinum*

Advisor: Patricia Champion, Dept. of Biological Sciences, University of Notre Dame

The bacterial pathogen *M. tuberculosis,* the causative agent of human tuberculosis (TB), results in an estimated 1.7 million deaths each year. In order to cause disease, the mycobacteria use the ESX-1 protein export system and associated substrates, which are essential for virulence in pathogenic mycobacteria. Recent work using clean deletions of substrate genes has found a continuum of ESX-1 secretion phenotypes, suggesting the widely accepted model of all substrates being essential for ESX-1 secretion is wrong. Additional studies using deletions of multiple substrates have revealed unexpectedly complex secretion phenotypes, suggesting that there are genetic interactions between not only individual substrates, but also involving the machinery of the ESX-1 system. Understanding the relationships between individual ESX-1 substrates and the secretion of virulence factors will allow us to better understand the molecular mechanisms of virulence factor secretion and pathogenesis of mycobacteria. For these studies, we completed a collection of strains bearing genetic deletions of individual substrate genes and their complements in the ESX-1 model organism *M. marinum.* Deletion strains and complements were analyzed for virulence by hemolytic assay and for secretion by western blotting. Virulence and secretion of each strain was interpreted in relationship to each other, their complements, and wild type and Δ*eccCb*$_1$ (ESX-1 deficient) controls. Changes in quantity and composition of total secreted protein populations are being studied using label free quantitative (LFQ) mass spectrometry. When complete, these studies will provide essential details about the function of the ESX-1 system, which will, in turn, inform the development of new tools for diagnosing, treating, and preventing TB.

CARMODY, ERIN (8)

Effects of the Obesity-Regulating Protein Gastrokine 1 on the Composition of the Microbiome

Erin Carmody
College of Science
Biological Sciences
Advisor: David Boone, Indiana University School of Medicine – South Bend, Harper Cancer Research Institute, and University of Notre Dame, Dept. of Biological Sciences

Gastrokine 1 (GKN1) is an 18 kDa mucosal protein produced exclusively in the antrum of the stomach. It is highly conserved across mammalian species. Although the function of GKN1 has not been elucidated, it does contain a BRICHOS domain that may mediate binding of GKN1 to microbes. We have generated Gkn1-/- mice that exhibit a lean phenotype but are otherwise healthy on a high fat diet. The $Gkn1^{+/+}$ (wild-type (WT)) mice gain significant amounts of weight on the same high fat diet. Thus, Gkn1 plays a role in diet-induced obesity. We hypothesized that interactions between GKN1 and bacteria in the gut microbiome are important in mouse lipid metabolism and obesity. Previously, the lab has performed 16S rRNA gene amplicon sequencing data of the different locations of the GI tract of WT and $Gkn1^{-/-}$ mice. Using QIIME, we analyzed these data to identify and compare organisms in the microbiomes. Further analysis using R identified the significance differences between organisms identified from QIIME. We expected to find differences between the presence and quantities of bacteria in WT and $Gkn1^{-/-}$ mice 16S rRNA.

Initially, the Greengenes database was used to analyze the 16S rRNA data as it is most easily utilized by QIIME and RStudio. It was last updated in 2013 and is not as up to date as the SILVA database, last updated in Spring 2018. Using the SILVA database, the 16S rRNA data was analyzed to better distinguish the bacteria and have more accurate results. Results showed significant differences between the class *Erysipelotrichia* in WT and $Gkn1^{-/-}$ mice. The WT mice had a significantly higher relative abundance of *Erysipelotrichia* as compared to the Gkn1-/- mice. *Erysipelotrichia* is part of the phylum Firmicutes, containing many subclasses known to be common in the gut microbiome and increased in mice consuming high fat diets. In the future, our goal is to understand how Gkn1 regulates *Erysipelotrichia* abundance in the gut and manipulate this process to prevent or reverse obesity.

CHUNG, HENRI (ORAL PRESENTATION)

Hydraulic residence time is a significant driver of metabolic activity in lakes

Advisor: Stuart Jones, Dept. of Biological Sciences, University of Notre Dame

Previous research has found that a lake's hydrologic characteristics, such as its hydraulic residence time (HRT) greatly influences its metabolic dynamics and its role in the global carbon cycle. In this study, we evaluated the effect of HRT on measures of lake heterotrophy and terrestrial dissolved organic carbon (t-DOC) mineralization in a whole ecosystem manipulation. We expected that a decrease in HRT would result in an increase in lake respiration and CO_2 concentration as the supply of labile t-DOC would be replenished at a quicker rate. We also, at the laboratory-scale, consider the potentially interacting effects of t -DOC quality and HRT. We hypothesized that the effect of carbon lability on respiration is dependent on HRT, with low HRT in addition to highly labile carbon having the greatest effect on rates of heterotrophic respiration. Our results suggest that hydraulic residence time play an important role in lake metabolism, significantly increasing respiration and CO_2 concentrations in our treatment pond. Furthermore, this effect was greater than the effect of varying t-DOC quality on respiration. We conclude that HRT is an equally if not more significant factor to lake respiration than the quality of imported t-DOC, and is an invaluable metric for assessing metabolic behavior.

CLARK, ELEANOR (9)

A novel Tfap2a genetic regulatory network drives distal nephron differentiation in zebrafish

Advisor: Rebecca Wingert, Dept. of Biological Sciences, University of Notre Dame

The kidney is responsible for nutrient reabsorption, fluid homeostasis, and waste excretion. Nephrons are renal functional units comprised of discrete populations of epithelial cells patterned into a series of proximal and distal segments with unique physiological functions. To establish targeted therapeutic approaches to ameliorate renal disease, it is imperative to understand the molecular mechanisms underlying nephron segment development. *Transcription factor AP-2 alpha* (*tfap2a)* is a novel regulator of a genetic network controlling distal segment differentiation in zebrafish. Here, using the *terminus* (*trm*) mutant model, which harbors a loss of function lesion in *tfap2a*, we identified three gene network factors: *sall1a*, *kctd15a*, and *kctd15b*. *Spalt-like transcription factor 1a* (*sall1a)* was determined to be a candidate for the *tfap2a* regulatory network based on its role in segment development in mammals. We found that $trm^{-/-}$ mutants exhibit elevated pronephric *sall1a* expression. Further, *sall1a* knock down in $trm^{-/-}$ results in decreased *romk2* expression, which marks the distal early (DE) segment. These data suggest potential genetic synergism between *tfap2a* and *sall1a* to promote DE development. *Potassium channel tetramerization domain containing 15a and 15b* (*kctd15a, kctd15b*) were also examined as *tfap2a* network components, since these proteins have been shown to repress Tfap2 proteins during neural crest ontogeny. Knock down of *kctd15a* or *kctd15b* initiated a drastic expansion of DE segment differentiation markers, indicating that these repressors are potent regulators of this nephron cell type. Continued studies are aimed at further dissecting the complex genetic interactions of *sall1a*, *kctd15a,* and *kctd15b* within the *tfap2a* network.

COMMINS, MARY (10)

The role of hydrology in understanding lake nutrient stoichiometry

Advisor: Carly Olson, Dept of Biological Sciences, University of Notre Dame

Lake ecosystems are biogeochemical hotspots that play an important role in global nutrient cycling. Lakes actively process nutrients, such as carbon (C), nitrogen (N), and phosphorus (P), that are received from their catchment. Therefore, catchment characteristics have important implications for fundamental lake ecosystem processes such as nutrient cycling and whole-lake metabolism. Specifically, lake hydrologic regimes often dictate nutrient loads entering lake ecosystems which can regulate nutrient limitation of ecosystem processes. Nutrients are strongly dependent on each other because they are linked through biotic metabolic demands and thus, have been studied using stoichiometric ratios. However, there is little understanding in how lake nutrient stoichiometry varies at the ecosystem scale and how major precipitation events alter the nutrient load stoichiometry of streams entering lakes. We hypothesized that lakes with contrasting drainage ratio (DR; the ratio of lake catchment area to lake area) will have different load and in-lake nutrient stoichiometries and that both stoichiometries will be altered during increased precipitation. Using data from two lakes in northern Wisconsin with contrasting DR, we calculated average stream nutrient load and in-lake nutrient stoichiometry (C:P, C:N, and N:P) across three years. Our findings include that the lake with the larger DR had higher C:P, C:N, and N:P nutrient loads, but had comparable in-lake nutrient stoichiometries to the lake with a smaller DR. This suggests a higher rate of C and N mineralization, or an increase in internal cycling of P in lakes with larger DR consistent with literature. Additionally, high stream discharge, an effect of extreme precipitation, preferentially exports C relative to N and P in both lakes. Further research in ecosystem stoichiometry may help to reveal the relative importance of ecosystem processes and increase our understanding of lake nutrient cycling particularly in the face of environmental change.

CONROY, MEGHAN (11)

Generation of AMIGO2^{KO} Ovarian Cancer Cell Line using CRISPR/Cas9 Technology

Norman Jin[1,4], Meghan Conroy[1, 4], Emily Franz[1, 2], Jing Yang[1, 2], Annamarie Bryant[1, 2] , Yueying Liu[1, 2] and M. Sharon Stack[1,2, 3]

[1]Harper Cancer Research Institute, [2]Department of Chemistry and Biochemistry, [3]Department of Biological Sciences,[4]Department of Preprofessional Studies, University of Notre Dame, Notre Dame, IN 46556

Ovarian cancer (OvCa), the most lethal gynecological malignancy in the United States, has a 5-year survival rate of less than 30% for late stage disease. New treatment targets are urgently needed. One approach to identify critical targets and processes involved in OvCa tumorigenesis is gene expression profiling using relevant OvCa cell lines, such as OVCAR5, a high-grade serous ovarian cancer (HGSOC) human cell line. We developed a highly aggressive derivative of parental OVCAR5 (OVCAR5-RFP-ip3) cells by culturing intra-peritoneal metastases recovered from mice *in vitro* and then transplanting the cultured cells *in vivo*. Carrying out this cycle three times, we selected for OVCAR5 cells with increased metastatic potential. RNA-seq analysis identified a novel target, Adhesion Molecule with Ig-Like Domain (AMIGO2) gene, as highly expressed in OVCAR5-RFP-ip3 cells. A transmembrane protein involved in cell-cell adhesion and angiogenesis, AMIGO2 plays a regulatory role in the PDK1-Atk signaling pathway. Alterations to this pathway caused by the upregulation of AMIGO2 can contribute to metastatic disease. To further study the functional effects of AMIGO2 on OvCa metastasis, we used the precise genome editing tool CRISPR/Cas9 to induce AMIGO2 gene knock-out in OVCAR5-RFP-ip3 cells. We designed four different single guide RNAs (sgRNAs) of AMIGO2, each able to form ribonucleoprotein (RNP) complexes with Cas9 nuclease. The assembled RNP complexes were separately introduced into OVCAR5-RFP-ip3 cells using Lipofectamine CRISPRMAX transfection reagent. Genome editing efficiency of the four sgRNA edited pools was measured by Sanger sequencing and ICE (Inference of CRISPR Edits) analysis. The highest sgRNA-edited cell pool was selected for single cell clonal expansion using single cell sorting by flow cytometry. Gene mutation and expression was further determined by sequence analysis, qPCR, and immunoblotting. The resulting OVCAR5-RFP-IP3$^{AMIGO2\ KO}$ cell model will facilitate further functional assays, contributing to an integrated understanding of OvCa metastasis, revealing new targets for therapeutic intervention.

CUNNIFF, PATRICK (12)

A Three Pronged Approach to understanding the defensive mechanisms in Green Ash (*Fraxinus pennsylvanica*) resistant to Emerald Ash Borer (*Agrilus planipennis*).

Advisor: Jeanne Romero-Severson, Dept. of Biological Sciences, University of Notre Dame

Emerald ash borer (EAB, *Agrilus planipennis*), an accidentally introduced Asian beetle, poses an acute threat to the native *Fraxinus* species in North America. Mass mortality in green ash (*F. pennsylvanica*) and white ash (*F. americana*) affects broad swaths of the landscape, from forests and farmland to urban streets, costing upwards of 1.7 billion dollars in 2011 alone. However, a few green ash (<1%) termed "lingering ash" have survived for years even after all other local green ash have died. In order to study the functional basis for resistance to EAB in lingering green ash, we have employed transcriptomics, proteomics, and metabolomics approaches to examine differences in gene expression, proteins, and secondary metabolites in susceptible green ash vs. lingering green ash. We analyzed 200 progeny from lingering x lingering and susceptible x susceptible crosses in twelve different families to find indicators and mechanisms of resistance. The goal is development of a test that accurately predicts resistance from a small tissue sample. This test will allow more accurate identification of potential lingering trees from the wild and enable incorporation into a selective breeding program to produce trees with durable long-term resistance to EAB. By increasing the rate at which defensive traits in ash can be selected for in a targeted breeding program, we can produce ash with enough resistance for restoration of the green ash resource across its native range.

DECKER, MEGAN (13)

Plasmid design for RNAi of retromer complex proteins in *Aedes aegypti* retina

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

The aim of the study was to create vectors for the knockdown of vacuolar protein sorting-associated proteins, Vps29p and Vps35p, via RNA interference (RNAi) in the retina of *Aedes aegypti*. These proteins are part of the *Aedes* retromer complex, which is thought to be involved in rhodopsin transport in the retina. Two sets of 21 base pair oligonucleotides were designed that coded for artificial microRNAs for Vps29 and Vps35 modeled after a successful approach used in *Drosophila*. These synthetic genes were flanked by an EcoR1 restriction site at the 5' end and a Nhe1 restriction site at the 3' end. Complementary oligonucleotides were annealed and inserted into the *Drosophila* pValium20 plasmid. The ligated plasmids were then transformed into *E coli*, cultured, and DNA from several colonies was analyzed. Restriction enzyme digest and gel electrophoresis followed by DNA sequencing confirmed the successful creation of the desired plasmid. Future studies will involve cloning a portion of the new vectors into a plasmid containing a promoter active only in the retina of *Aedes.* Transgenic animals created by introducing this plasmid into mosquitoes will then allow characterization of the effects of Vps knockdowns on movement of the major *Aedes aegypti* rhodopsin, *Aaop1*. This analysis will make use of antibody staining and confocal microscopy.

DEL GRECO, CHRISTINA (ORAL PRESENTATION)

Identifying potential target genes to optimize cisplatin chemotherapy through the *SNAIL* pathway

Advisor: Amy Stark, Dept. of Biological Sciences, University of Notre Dame

Cisplatin is a common platinum chemotherapy treatment given to breast cancer patients, but it is plagued with non-response and resistance. Much research has been focused on trying to understand and improve therapy hurdles. One promising avenue is the *SNAIL* pathway, which has complex roles throughout the cell. Given the knowledge of the cisplatin mechanism, we hypothesized that gene expression changes seen after *SNAIL* upregulation would be reversed after cisplatin treatment. In order to investigate this prediction, we analyzed gene expression in MCF-7 cells in response to upregulated *SNAIL* as found in the Expression Atlas. The fourteen genes with the lowest p-values for expression changes in response to *SNAIL* overexpression (p=1.88e-8) were then researched to prioritize the most promising targets for cisplatin therapy modification. Genes selected for initial study were *THBS1*, *S100P*, *LDHB*, *DECR1*, *TSPYL5*, *TMEM47*, *TACSTD2*, *HOXA9*, *AKT3*, *UPK2*, and *H2AFJ*. qPCR was performed to assess the expression changes in each gene when cells are exposed to 5 uM cisplatin treatment for 24 and 48 hours. Resulting expression changes showed some cases of overall increases in expression, such as *S100P*, cases of overall decreases in expression, such as *TSPYL5*, and cases of dynamic changes in expression, such as *THBS1* and *AKT3*. Future research will be aimed towards applying these expression changes towards optimizing cisplatin chemotherapy outcomes by inhibiting target genes that likely play a role in worsening breast cancer prognoses.

DEUTSCH, JESSICA (14)

Selective Capture of Herceptin by mAb K19 on Chemically Modified Membranes and Wafers

Advisor: Merlin Bruening, Dept. of Chemical and Biomolecular Engineering, Dept. of Chemistry and Biochemistry

Monoclonal antibodies (mAbs) are a rapidly growing class of pharmaceutical drugs and their high specificity and affinity lead to remarkable efficacy in cancer therapy. Concentrations of therapeutic antibodies in blood vary more than 4-fold among patients. Increased concentrations of mAbs can result in unwanted side effects while low levels will lead to ineffective treatments. Development of methods that rapidly and inexpensively determine serum mAbs concentration will aid in tailoring dosages to specific needs and avoid over-prescription of these costly treatments. Recent work with Herceptin (Trastuzumab), a common breast cancer antibody treatment, suggests that functionalized membranes can isolate this protein from serum with ~70% purity. Nonspecific interactions between other proteins in serum and the functionalized membrane lead to the 30% contamination, which precludes precise analyses of low concentrations of Herceptin. This project focuses on decreasing nonspecific adsorption to membranes functionalized with the peptide KGSGSGSQLGPYELWELSH (K19). Herceptin was isolated by passing serum through a functionalized membrane including a protease and a mimotope, which chemically mimics the epitope, or binding region, of the antigen. The epitope region of K19 mimics the HER2 receptor to selectively capture Herceptin. The first step, which included varying the pH of the loading buffer from pH range 5-8 did not fundamentally decrease non-specific absorption. Addition of detergents in the wash stages meant to improve elution methods to enhance the selective recovery of Herceptin yielded no significant change. Current work using chemically modified gold wafers functionalized with K19 at decreasing concentrations is promising. This work is based on a trend seen in small molecules; that at lower concentrations of bound mimotope, a higher binding concentration is observed. Preliminary results of Herceptin binding reflect this trend. The next step in this experiment will test whether non-specific binding from serum spiked with Herceptin decreases at lower K19 concentrations.

DULAL, CHRISTINA (15)

ICEBall

S. Y. Strauss, A. Aprahamian, C. Casarella, P. Fasano, B. Frentz, K. Manukyan, C. Reingold, M. K. Smith, and W. Tan
University of Notre Dame
S. R. Lesher, C. Hughes, X. James, M. Lowe, and E. Temanson
University of Wisconsin - La Crosse

The project I am currently working on is the Internal Conversion Electron Ball Array, also known as ICEBall. ICEBall is designed to explore the usage of internal conversion electrons, instead of photons, to measure 0+ states. Within the Nuclear Lab, we will further explore the 0+ excited states of Gadolinium isotopes on enriched Samarian targets at 16-21 MeV. Through this experiment, we will also determine optimum beam energy when using enriched targets through certain energy channels. Physically, ICEBall is a spherical chamber containing 6 Si(Li) detectors that detect conversion electrons influenced by the nucleus and 2 liquid scintillators that detect the particles knocked off the isotope at a certain energy level, which is never high enough to destroy the HPGe detectors due to neutron flux.

With regards to my personal contribution, I worked on the magnet structure that will be inside of ICEBall, directing particles toward the Si(Li) detectors. My work involved repairing a disabled vacuum chamber to be fully functional and designing/constructing various mechanisms to model the interior of ICEBall and support the magnet designs being tested. In the future, we will begin testing these magnets inside of the model chamber. If a new magnet design is found to be more efficient, additional mechanisms will have to be constructed in order to house those new magnets for further testing. After the most efficient magnet is discovered, experimentation of internal conversion electrons in ICEBall can be conducted.

Note: This work is supported by COS-SURF and the NSL via the NSF under grant No. PHY-1713857

EGAN, BAILEE (ORAL PRESENTATION)

Investigating the Associations Between the Prokaryotic and Eukaryotic Gut Microbiomes in Long-tailed Macaques (*Macaca fascicularis*)

Advisor: Hope Hollocher, Dept. of Biological Sciences, University of Notre Dame

While prokaryotes of the primate gut microbiome have been well-studied, the eukaryotic component is largely uncharacterized, unrecognized, and misunderstood. Mounting evidence is showing that the eukaryotic microbiome is more diverse and complex than initially anticipated. Previous work in long-tailed macaques has identified over 800 eukaryotic genera and indications of food webs among the trophic guilds. Moreover, eukaryotes are likely to be commensal members, not pathogens, of the gut—where traditional parasites, such as *Blastocystis*, have been found in healthy humans. Taken together, eukaryotic symbionts are likely to interact with the prokaryotic microbiome. Therefore, we investigate the associations between these two groups in long-tailed macaques using *16S rRNA* and *18S rRNA* metabarcoding to characterize the prokaryotic and eukaryotic resident taxa in the gut. We find that the composition of the prokaryotic and eukaryotic microbiomes is highly variable, even among individuals of the same population. Although there was no correlation between overall eukaryotic and prokaryotic diversity, multiple genera were strongly associated with changes in prokaryotic diversity. We also characterize profiles of the prokaryotic microbiome using enterotypes to determine whether eukaryotic resident taxa are associated with these profiles. Although the composition of eukaryotic resident taxa was not a significant factor in shaping these enterotypes, specific eukaryotes were identified to be associated with enterotypes. Our findings suggest that while there is little association between the eukaryotic and prokaryotic components of the gut microbiome, there are specific eukaryotic groups that have strong associations with the prokaryotic microbiome and may play important ecological roles in the gut.

FINK, ANN (16)

Title: "Influence of fish behavior on angler catch rates in a temperate freshwater lake"

Advisor: Colin Dassow, Dept. of Biological Sciences, University of Notre Dame

Previous research has found that largemouth bass, upon repeated sampling and use of mark and recapture tracking method, exhibit homing tendencies, important to understanding angling pressures on fish caught more than once within a lake. Previous studies have additionally shown that mortality rates are not significantly different in largemouth bass caught more than once, but it is unknown as to how specific fish behavior influences angler catch rate. This is important for predictability in fish populations, as well as management purposes. The objective of this study was to determine how fish may show differential preference for a specific habitat or geographical location within the lake, and how the location of anglers' catches reflect these preferences. We hypothesized that as abundance of largemouth bass declined throughout the three-month trial period, geographical catch locations would become more clustered. Using a mark-and-recapture method for population estimates, we were able to explore clustered catch rates at different population sizes. A controlled set of anglers with standardized gear took GPS locations of all catches (multiple and single) of 207 largemouth bass. Homing tendency was to be identified via individual fish tags. Plots were made of all fish that experienced multiple recaptures. Additional fish characteristics such as fish length were analyzed. A Ripley's K test was used to analyze spatial data. Ripley's K suggests repeated captures may be non-randomly distributed. This indicated that clustering may be a mechanism by which hyperstability can occur. This finding helps provide a clear mechanism by which anglers may maintain high catch rates on a declining abundance of fish through the intentional targeting of fish clustered in specific areas of a lake.

FITZ, DEVIN (17)

Impact of TREM2 deficiency on the phenotype of mice expressing human APOE3 and APOE4

Devin Fitz[1], Nicholas Fitz[2], Brittany Playso[2], Iliya Lefterov[2], Rada Koldamova[2]

[1]University of Notre Dame, Notre Dame, United States
[2] University of Pittsburgh, Department of Environmental and Occupational Health, Pittsburgh, United States

The strongest known genetic risk factor for late-onset Alzheimer's disease (AD) is the inheritance of ApolipoproteinE4 (APOE4). Usually APOE enhances proteolytic breakdown of Aβ and/or facilitates its clearance, the main component of senile plaques that are present in Alzheimer's disease patients. *APOE4/4* carriers have a ~12-fold higher incidence of AD, decreased age of onset, increased Aβ deposition and lower APOE levels. Specific disease variants in the triggering receptor expressed on myeloid cells 2 (*TREM2*) gene have been identified by GWAS as potential risk factors for AD. *TREM2* encodes a receptor of the innate immune system that normally interacts with microglia via a signaling pathway to either trigger Aβ phagocytosis or to instruct microglia to the site of neurodegenerative damage. TREM2 variants show reduced uptake of beta-amyloid complexes by microglia and decrease in plaque associated microglia, increasing the size and number of plaques, thus modulating differential aspects of AD pathology. Results from recent studies suggest that there is a link between the two proteins, where TREM2 binds APOE in an isoform specific manner. This could significantly influence microglia-mediated function, however, the biological significance, and the interconnected role of TREM2 and APOE in AD pathology, is not well understood. We hypothesize that APOE isoforms and Trem2 function interact to differentially affect the size and quantity of beta-amyloid plaques and density of surrounding microglia. To test the hypothesis, brain tissue was collected from APP/PS1 mice expressing APOE3/Trem2^{WT}, APOE4/Trem2^{WT}, APOE3/Trem2^{KO}, APOE4/Trem2KO and histological analysis of amyloid deposition (6E10, Thioflavin S) and microglia reactivity (IBA1) was examined. This study substantially increases our understanding of the interaction between APOE isoforms and TREM2 in association with AD pathology.

FRANZ, EMILY (18)

Obesity's Impact on Cancer: Stimulation of SREBP1-Regulated Lipogenesis by Lysophosphatidic Acid in Human Ovarian Cancer Cells

Emily Franz[1, 2], Norman Jin[1, 4], Meghan Conroy[1,4], Jing Yang[1, 2], and M. Sharon Stack[1,2, 3]

[1]Harper Cancer Research Institute, [2]Department of Chemistry and Biochemistry, [3]Department of Biological Sciences,[4]Department of Preprofessional Studies, University of Notre Dame, Notre Dame, IN 46556

Women with ovarian cancer display a unique mechanism of intra-abdominal metastasis that has already occurred in 80% of women at the time of diagnosis, making it the leading cause of death from gynecological malignancy. Obesity and the accumulation of adipose tissue are known to increase the risk of high grade serous ovarian cancer (HGSOC) progression. With 66% of U.S. women overweight, an investigation into obesity risk factors associated with ovarian cancer is critical. We recently showed that tumors grown in mice on a western diet (40% fat) displayed a striking increase in nuclear-localized sterol regulatory element binding protein 1 (SREBP1) and intracellular lipid content compared to the control. SREBP1 is a master transcriptional regulator of *de novo* lipogenesis that can induce lipogenic reprogramming of tumor cells. SREBP1 is synthesized in the ER and transported to the Golgi via SREBP cleavage-activating protein (SCAP) wherein it undergoes regulated proteolysis, releasing the active transcription factor. To evaluate SREBP1 as a potential therapeutic target for ovarian cancer in the obese host, our experiments used the small molecule inhibitor Fatostatin, which blocks lipogenesis by inhibiting SCAP-mediated transport of SREBP1 to the Golgi. Furthermore, lysophosphatidic acid (LPA) is a bioactive lipid mediator highly expressed in ascites of ovarian cancer patients that may stimulate SREBP1 pathways. To determine whether LPA may be a microenvironmental mediator of adipose:tumor cross-talk, we have incubated human HGSOC cell lines, OVCAR5 and OVCAR8, with LPA in the presence or absence of Fatostatin, and examined SREBP1 expression and nuclear translocation. Our data showed that, while Fatostatin treatment blocks the processing and nuclear transport of SREBP1, LPA induces SREBP1 expression in dose- and time-dependent manners. These results support the hypothesis that LPA plays an important role in tumor *de novo* lipogenesis through SREBP1 and its downstream transcriptional pathways in ovarian cancer cells.

GAONA, JOCELYN (19)

Adenomatous Polyposis Coli regulates transcriptional activity of Epithelial Membrane Protein 2

Jocelyn Gaona 1, 2, Alyssa Lesko 1, 2, Carolyn Ahlers 1, 2, Anna Lyons 1, 2, Jenifer Prosperi 1, 2, 3

1 Department of Biological Sciences, Harper Cancer Research Institute, University of Notre Dame, Notre Dame, United States
2 College of Science, University of Notre Dame, Notre Dame, United States
3 Department of Biochemistry and Molecular Biology, Indiana University School of Medicine – South Bend, South Bend, United States

Adenomatous Polyposis Coli (APC) is a tumor suppressor that regulates polarity proteins. Epithelial structure and intracellular signaling are disrupted by the loss of apical-basal polarity and act as an early marker for tumor development. In 3D Matrigel culture, we illustrated that APC knockdown (APC KD) in Madin-Darby Canine Kidney (MDCK) cells resulted in inverted polarity and increased cyst size. The novel observation that Epithelial Membrane Protein 2 (EMP2) expression was increased upon APC loss was made through microarray analysis. Knockdown of EMP2, a tetraspan protein that is upregulated in several epithelial cancers, in APC KD cells normalized cyst size and apical polarity, suggesting a previously unknown role for EMP2 in the regulation of cyst development. The downstream mechanisms are important in investigating the underlying methods that lead to the disruption of polarity in cells. Based on 2D Gel Electrophoresis, we investigated the expression of Histone H3.3, ERAB, and AKT through Western Blot analysis. Our results showed no significant difference between the wild type MDCK and APC KD MDCK cell lines for Histone H3.3, ERAB, or AKT. We also looked at localization of both plectin and filamin through Immunofluorescence, and demonstrated that there was no significant difference in localization for neither plectin or filamin. In addition, we are investigating which specific portions of APC are involved in polarity via site directed mutagenesis (SDM). We have created constructs with the EB1 region successfully deleted and are currently creating constructs with the Actin/Microtubule/Actin domain deletion, the Actin/EB1 domain deletion, and the Actin/Microtubule domain deletion. Future studies will use these constructs to reintroduce APC, lacking specific binding partners, back into APC KD MDCK cells to observe what controls polarity. By understanding the interaction of APC and EMP2 and the influence on apical polarity, we will identify the key players in APC disease progression.

GEORGIADIS, REBECCA (20)

MAPK pathway expression in platinum-treated cancers

Advisor: Amy Stark, Dept. of Biological Sciences, University of Notre Dame

The Mitogen-Activated Protein Kinase (MAPK) Pathway is a critical cell signaling pathway in normal cell function. It is involved in cell proliferation, cell survival, and differentiation. It is a commonly mutated pathway in many cancers, and drug targets have already been tested in clinical trials for many components of this pathway. Further understanding of how gene expression in this pathway is altered by treatment of chemotherapeutic agents can potentially impact resistance to chemotherapeutic agents. The half-maximal inhibitory concentration (IC50) was found for A549 cultured lung adenocarcinoma cells and HCT116 cultured colorectal carcinoma cells treated with cisplatin. The IC50 concentration of cisplatin-treated A549 cells was 5.429 μM and of HCT116 cells was 4.42 μM. Therefore, the HCT116 cell type is more sensitive to this chemotherapy. qPCR was then conducted on platinum-treated A549 cultured cells and HCT116 cultured cells to evaluate expression of 6 MAPK pathway genes: RAF1, MAP2K1, MAPK1, STAT1, CREB1, and LAMTOR3. A different pattern of induced gene expression was observed across all three cell types. The 24 hour time point of cisplatin-treatment of A549 cells demonstrated a consistent upregulation of expression in all genes, which is starkly contrasted with a significant downregulation at the 48 hour time point. In HCT116 cells, cisplatin treatment led to the opposite trend, as there was downregulation at the 18 hour time point and significant upregulation at the 48 hour time point. This demonstrates that level of expression of genes in the pathway is cell-type dependent and time-dependent. Naringenin is a flavonoid that has been implicated in MAPK signalling. We tested this compound as an inhibitor to determine the effect on platinum-induced gene expression in lung and colorectal cells. These results have implications for treatment of multiple cancers, especially lung and colorectal cancer.

GERSTBAUER, ERICA (21)

Direct Stimulation of STARD9 as a Novel Therapeutic for Niemann Pick Type C Disease

Advisor: Kevin Vaughan, Dept. of Biological Sciences, University of Notre Dame

Although extracellular transport of cholesterol is well-understood, not much is known about the intracellular transport of cholesterol. Niemann Pick Type C disease reveals some novel mechanistic details about cholesterol transport because transport from the lysosomal lumen to the endoplasmic reticulum is impaired in this disease. The Vaughan lab identified lysosomal tubulation as a novel mechanism for cholesterol transport. Furthermore, lysosomal tubulation is driven by STARD9, a novel transmembrane kinesin with a sterol-sensing domain. Loss of this domain abolishes lysosomal tubulation, thereby linking STARD9 activity to cholesterol concentration. To test this hypothesis, our lab developed a novel Lysosomal Tubulation Assay. In this assay, cells are grown in sterol-free conditions, which abolishes tubulation, and LDL particles are added back to the media. Lysosomal tubulation is rescued by LDL in a time- and concentration-dependent manner. This led us to investigate which component of the LDL particles stimulates STARD9 to induce lysosomal tubulation. In this study, we examined the effect of three oxysterols on lysosomal tubulation and cholesterol metabolism: one which is made in the endoplasmic reticulum, one that comes in through the diet, and a third that is made in mitochondria. These oxysterols are found in LDL particles and have been implicated in cholesterol transport previously. We measured the oxysterols' effect on tubulation through our Lysosomal Tubulation Assay and confirmed this with an SREBP assay. These experiments reveal that the mitochondrial oxysterol was able to restore tubulation to physiological levels and significantly decrease nuclear SREBP, even at concentrations as low as 1μM. This work suggests that the mitochondrial oxysterol has the potential to act as a potent signaling molecule by binding to STARD9 and stimulating lysosomal tubulation, thereby motivating further investigation as a novel therapeutic for NPC Disease.

GIPSON, ROBERT (22)

Synthesis and Characterization of Iron Carbonyl-Functionalized CdS Nanocrystal

Robert Gipson, Keith Schival, Emily Y. Tsui
Department of Chemistry & Biochemistry, University of Notre Dame, South Bend, IN 46556.

Colloidal semiconductor nanocrystals play a promising role in the development of solar cells and biomedical imaging due to their strong, tunable light absorption and emission. We sought to functionalize the surface of a semiconductor nanocrystal with a spectroscopically active probe in order to obtain greater understanding of surface sites. In this work, we coordinated a tetracarbonyl ferrate complex to the surface of cadmium sulfide nanocrystals and used gel permeation chromatography to isolate the functionalized nanocrystals from carbonyl-containing byproducts. UV-Vis spectroscopy and pXRD support that there is no change in size distribution or crystallinity or the cadmium sulfide, and carbonyl peaks were observed via FTIR. This technique could be applicable in other model systems and may lend itself to surface trap site analysis.

GORMAN, NICOLE (23)

Quantifying the recovery of denitrification following restoration-related construction in an agricultural watershed

Authors: Nicole T. Gorman, Shannon L. Speir, Jennifer L. Tank, Ursula H. Mahl

Denitrifying bacteria carry out an important ecosystem function, permanently removing reactive nitrogen from streams and rivers and reducing nutrient loading to downstream ecosystems. Denitrification is a dissimilatory process in which nitrate (NO_3^-) is converted to dinitrogen gas (N_2). In the past, many studies have examined denitrification using the acetylene block (AB) method, measuring potential denitrification rates under optimized conditions. The AB method prevents the conversion of N_2O to N_2, allowing N_2O to accumulate and be measured using gas chromatography. For this reason, it can be difficult to extrapolate real-world N-removal from these potential rates. Recently, the use of sediment incubations paired with membrane inlet mass spectrometry (MIMS) has alleviated technological limitations of the AB method, allowing for the measurement of denitrification rates under more natural conditions. The MIMS method analyzes dissolved N_2 concentrations by measuring N_2:Ar ratios in water samples. Here, we collected stream sediments and soil samples from adjacent restored floodplains at Shatto Ditch (Kosciusko County, IN). By carrying out both assays, we compared denitrification rates under optimized conditions using the AB method and natural conditions using the MIMS method. We hypothesized that potential denitrification rates derived from the AB method would be higher than natural rates measured via MIMS assays. We were able to compare the two methods by regressing denitrification rates as determined by AB versus rates determined via MIMS assays, then comparing them to a 1:1 line. By quantifying differences between AB and MIMS denitrification rates, we can translate historical AB rates into rates we would expect to observe under more natural conditions. These results can help constrain global nitrogen cycle models by updating estimates of stream and floodplain denitrification rates and will allow researchers and managers to better assess the role of denitrification in nutrient management efforts.

GOZUN, MELISSA MALIA (ORAL PRESENTATION)

A novel quinazolinone with improved oral bioavailability and *in vivo* efficacy against methicillin-resistant *Staphylococcus aureus*

Melissa Malia N. Gozun, Zhihong Peng, Jeshina Janardhanan, Yuanyuan Qian, Valerie A. Schroeder, William R. Wolter, Shahriar Mobashery, and Mayland Chang

Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, IN 46556

As the challenges in the face of antibiotic-resistant bacterial infection, in particular methicillin-resistant *Staphylococcus aureus* (MRSA), have increased, so has the need to discover novel antibiotic treatments. One potential treatment for these bacterial infections is the novel quinazolinones, a class of antibacterials with *in vitro* activity and *in vivo* efficacy against MRSA. Optimization of the lead quinazolinone (compound **1**) led to the discovery of compound **2**, with 4-fold improvement in minimal-inhibitory concentration (MIC) against *S. aureus*. A bioanalytical method using UPLC with UV detection was developed to measure the levels of compound **2**. Compound **2** is stable in human plasma and human liver microsomes and has plasma protein binding of 95.4 ± 0.02%. A pharmacokinetic study in mice shows that compound **2** has low clearance of 7.7 mL/min/kg and increased oral bioavailability of 65% . The compound shows *in vivo* efficacy in a mouse neutropenic thigh MRSA infection model. These results indicate that compound **2** shows promise for the treatment of MRSA infections.

GREIF, KEVIN (ORAL PRESENTATION)

Bend Consistency Cut Performance in the CMS Detector L1-Trigger Upgrade

Advisor: Kevin Lannon, Dept. of Physics, University of Notre Dame

As the Large Hadron Collider (LHC) upgrades to higher luminosity, more performance is demanded from the L1 Trigger system. An upgrade to the L1 Trigger known as the Track Trigger will provide this performance by incorporating data from the tracker into the L1 Trigger system. This requires quickly reconstructing the paths of particles using only the processing power available on Field Programmable Gate Arrays (FPGA). Given these limited resources, cutting down on the number of fake tracks (those that didn't come from a real particle) is important. This research seeks to do this by utilizing a quantity called bend, which gives a rough estimate of the direction of the particle as it passes through a sensor. Bend is used to implement a bend consistency cut, which requires that the bend of each signal on a possible track is consistent with the track's transverse momentum. First this cut was implemented, and then its performance was studied. Results suggest that this cut will greatly reduce the loss of tracks due to lack of resources, while throwing away only a trivial number of real tracks.

HANSEN, EMILY (ORAL PRESENTATION)

Insecticide resistance in *Aedes aegypti,* the primary vector of dengue and Zika in Belize, Central America

Emily Hansen, Nicole L. Achee
Department of Biological Sciences, Eck Institute for Global Health, University of Notre Dame, Notre Dame, United States

Aedes aegypti is a primary vector of various mosquito-borne diseases that affect the global community, typically living in low-middle income countries. Although insecticides can be an effective and common tool for reducing adult mosquito populations, increasing levels of insecticide resistance to four primary classes of chemicals recommended by the World Health Organization (WHO) for use in public health: carbamates, organochlorines, organophosphates, and pyrethroids, poses a significant threat to these products and therefore controlling disease in at-risk human populations, including Belize, Central America. The objective of this study was to evaluate the insecticide resistance status of *Ae. aegypti* from Orange Walk Town, Belize using standard WHO protocols and test procedures (WHO, 2e 2016). Assays were performed against WHO diagnostic doses of two chemicals commonly used in dengue vector control: Permethrin (a pyrethroid) applied through indoor thermal fogging, and Malathion (an organophosphate) applied through truck mounted spraying. Results using Permethrin (0.75%), indicated a corrected 90.3% 24-hour mortality in *Ae. aegypti* exposed test cohort suggesting the presence of resistant genes. However, according to WHO assay guidelines, additional tests must show a mortality below 98% to confirm resistance status. Further, when testing against malathion (5.0%) a 46.8% corrected 24-hour mortality in *Ae. aegypti* exposed test cohort confirmed the existence of resistant genes. However, given that less than the WHO recommended minimum sample size was evaluated (i.e., 100 mosquitoes), it is necessary to repeat assays with additional samples at the same dose before confirmation of resistance can be made and resistance intensity testing begins. Overall, the data collected thus far suggests that *Ae. aegypti* mosquito populations from Orange Walk Town, Belize may be resistant to two frontline vector control tools. The results from this study will be shared with the Ministry of Health Vector Control Division and be compared to data being generated by the Belize Vector Ecology Center (BVEC) to facilitate independent verification of in-country capacity.

HATFIELD, JESS (ORAL PRESENTATION)

A Quantitative Approach to Measuring Low Malic Acid Levels in Wine

Jess Hatfield, Holly Goodson

Malolactic fermentation (MLF) is a secondary fermentation process that occurs in most red and some white wines; knowing when this process is complete is essential in promoting wine stability and flavor/aroma, and preventing spoilage. The level of malic acid (MA) is often used as an indicator of when MLF is finished, with <0.05 g/L MA considered finished with MLF. Currently, there are no reliable, inexpensive, and straightforward methods of measuring MA at this low level. Thus, the current project was aimed toward exploring quantitative, reliable, and inexpensive methods to measure low levels of MA. Multiple methods were tested, and Accuvin test strips fit preliminary criteria of being reliable, accurate, and inexpensive. However, the results from the company provided procedure were mostly qualitative to semi-quantitative. Therefore, we developed an approach to straightforwardly quantify these test strip results, using ImageJ and Microsoft Excel. We then tested the precision of this method at critical MA levels of 0-0.10 g/L, corresponding to when the wine is nearing MLF completion. Results indicate that, when quantified according to our method, the Accuvin test strips were precise at low levels of MA (0, 0.025, 0.05, 0.075, 0.10 g/L), with average standard deviations of <0.005 g/L. At the same time, the quantified MA levels, while precise, were consistently different from those indicated on the provided company color charts at higher MA levels (0.05, 0.075, and 0.10 g/L). These results lead to two significant conclusions. First, Accuvin test strips, when used with our ImageJ/Excel quantification method, provide a quick, reliable method to precisely measure MA at low levels. Second, the Accuvin provided color charts used for quantification are slightly skewed at MA levels of >0.05 g/L. These findings will be useful for winemakers looking for straightforward, effective, and inexpensive quantification methods for measuring MLF completion.

HELMKE, ALEC (24)

Breaking the Chain: Enzymatic and Organic Colorimetric Detection of Caffeine as a Cutting Agent for Illicit Drugs

Alec Helmke, [1] Tracy- Lynn Lockwood, [2] Marya Lieberman [2]
[1] Department of History, Notre Dame, United States
[2] Department of Chemistry and Biochemistry, Notre Dame, United States

The field testing of illicit drugs including cocaine, heroin, and methamphetamine remains a challenging task for drug enforcement agents. Although these chemicals can be identified accurately in laboratory settings, test kits available for field testing are often unreliable, in part due to the use of cutting agents by drug manufacturers and dealers. Cutting agents mimic the appearance and physical attributes of the drug they are added to, allowing manufacturers and dealers to save money by lacing their drugs with less-expensive products. Caffeine—being inexpensive and producing similar physiological responses as some illicit stimulants—is one of the most common cutting agents used in the illicit drug trade. So common, in fact, that recent studies have listed caffeine as one of the top adulterants for ecstasy, methamphetamine, amphetamine, cocaine, and heroin. Yet, researchers have not adequately tested simple, field-ready tests for caffeine, and most caffeine tests utilize complex machinery, complicated procedures, and/or unreliable chemical reagents. Being able to test for caffeine in illicit drug samples would be a great advantage to drug enforcement officials, as cutting agents are often used to trace drug supply chains. As such, I endeavored to find a simple, colorimetric test for caffeine to apply to idPADs, paper analytical devices designed to be easy-to-use and dependable field tests for illicit drugs. I compared color tests involving xanthine oxidase enzyme and an organic coupling method called the Pauly Reaction. Results will indicate whether these solutions produced accurate and reliable colorimetric reactions that can be integrated effectively into idPADs.

Keywords: Paper Analytical Devices, Illicit Drug Field Testing, Caffeine, Colorimetric Tests

HERMANN, KALLIN (25)

Characterization of the Role of miR-106b in Human Oropharyngeal Squamous Cell Carcinoma (OPSCC) Progression

Kallin Hermann[1,2], Ryan Ward[1,2], J. Johnson[1,2] and M. Sharon Stack[1,2]
[1]Department of Chemistry and Biochemistry, [2]Harper Cancer Research Institute, University of Notre Dame, Notre Dame, IN

In the United States, 7.7 million adults harbor high-risk HPV in their oral cavity. HPV DNA is particularly relevant in its correlation with incidence of HPV-associated oropharyngeal squamous cell carcinomas (OPSCC). The importance of studying HIV-associated OPSCC is critical as its frequency is projected to surpass that of cervical cancer by 2020. In the Stack Lab, the long term goal of oral cancer research is to gain deeper understanding of OPSCC progression and to determine specific molecules, structures and cellular events that can be used as targets for future treatments of prevention. In this study, the role of miR-106b in OPSCC progression will be characterized. Human palatine tonsillar tissue and palatine tonsillar cell cultures will be used to observe the interaction of HPV+ cells (which express miR-106b), HPV- cells (which do not express miR-106b) and cells which have been manipulated to express or knockdown miR-106b expression.

HERMANN, NATHAN (ORAL PRESENTATION)

Influence of the Pacific Salmon Spawning Subsidy on the Feeding Ecology and Growth of Great Lakes Stream-Resident Trout

Nathan T. Hermann[1], Dominic T. Chaloner[1], Brandon S. Gerig[2], and Gary A. Lamberti[1]
[1]University of Notre Dame, Department of Biological Sciences
[2]Northern Michigan University, Department of Biology

Pacific Salmon (*Oncorhynchus* spp.), like many migratory animals, strongly influence the ecosystems into which they migrate. Salmon spawners influence streams by providing resource subsidies of nutrients and energy while also acting as ecosystem engineers through benthic disturbance. In the Great Lakes region, non-migratory non-native Brown Trout (*Salmo trutta*) and native Brook Trout (*Salvelinus fontinalis*) reside in many of these streams that receive salmon resource pulses. To understand the feeding strategies of resident fish exposed to a salmon-derived resource pulse, we quantified Brook and Brown Trout diets before and during salmon spawning. We also conducted a laboratory feeding trial to monitor the anatomical, behavioral, and physiological responses to different feeding regimes. Data from the survey and experiment informed an individual-based bioenergetics model (IBM) to explore different behaviors affecting resource pulse exploitation. Survey results showed that trout, regardless of species, consumed 4.5-fold more mass during salmon runs (GLM, $p<0.001$), primarily as eggs (61.2 +/- 40.5% of consumption). Laboratory experiments showed Brook Trout grew ~10x more than Brown Trout (ANOVA, $p<0.001$), due to a 37% higher conversion efficiency (GLM, $p=0.049$), despite similar isotopic enrichment (GLM, $\delta^{15}N$ $p=0.084$; $\delta^{13}C$ $p=0.988$) and tissue percent dry mass (ANOVA, $p=0.387$), a proxy for energy density. Gorging corresponded to a near doubling of stomach volume (ANOVA, $p<0.001$), suggesting physiological changes facilitated their growth. Furthermore, our IBM found that active foraging combined with gorging enables the consumption levels that support the highest growth (ANOVA, $p<0.001$). Overall, our study found that trout can alter their feeding responses during a resource pulse, indicating optimal foraging can be sensitive to variation even with abundant resources. This may be particularly important for fisheries management of Brown Trout given their low conversion efficiency that requires high resources which can be provided by migratory spawners such as introduced salmon or native White Suckers (*Catostomus commersonii*).

HIPP, REBECCA (26)

Expression of *her* genes during the reprogramming of Müller glia in zebrafish retinal regeneration

Advisor: David Hyde, Dept. of Biological Sciences, University of Notre Dame

The zebrafish retina is highly similar to the mammalian retina in structure and organization. However, the zebrafish retina can undergo a robust regenerative response upon any injury resulting in significant reduction of retinal neurons. Müller glia, a subtype of radial glial cells specific to the vertebrate retina, are induced upon damage to dedifferentiate and reenter the cell cycle to produce multipotent neuronal progenitor cells (NPCs). The NPCs proliferate before migrating to the region of damage, where they differentiate into the appropriate retinal cell types. The *her* genes have been well-documented as targets of the Notch signaling pathway, which has been shown to regulate Müller glia quiescence and proliferation in retinal regeneration. Previous studies in zebrafish neuronal development have demonstrated that *her* genes maintain neuronal progenitors in an undifferentiated state. In order to investigate the role of *her* genes in the reprogramming of Müller glia, I generated expression patterns using quantitative RT-PCR during Müller glia dedifferentiation. In addition, I investigated expression of candidate *her* genes following morpholino-mediated knockdown of Notch3, which has been shown to maintain Müller glia in a quiescent state. Most *her* genes tested were upregulated soon after the start of retinal damage, indicating a potential role in the early phases of regeneration. Alternatively, *her6*, *her8a*, and *her9* were found to be predominantly downregulated. The knockdown of Notch3 appeared to have differential effects on the expression of *her1, her8.2,* and *her13* suggesting that *her* genes may be differentially regulated by Notch3 during regeneration. Further investigation into the significance of these genes towards NPC formation and proliferation could offer insight into the overall mechanism through which regeneration of neuronal cells is possible in zebrafish.

HOUSSEIN, FIRAS (27)

Prey Documentation of Bald Eagles and their Eaglets at ND-LEEF

Firas Houssein, Brett Peters, Michael Brueseke, and Gary Lamberti

A live in-nest digital camera has filmed a Bald Eagle (*Haliaeetus leucocephalus*) nest at the Notre Dame Linked Experimental Ecosystem Facility (ND-LEEF) in St. Joseph County, IN since 2017. This camera transmits high-resolution video and images from eagle nest-building to egg incubation, and through eaglet fledgling. On April 2, 2018, two eaglets hatched in the nest, as recorded by the in-nest camera. Beginning on April 6, the in-nest camera was programmed to take still shots of the nest every 20 minutes throughout the day. Each picture was automatically sent to a file in Google Drive and examined for the presence of prey items, which were identified to the lowest taxonomic level possible, most often the genus or species level. A total of 135 prey items were recorded in the 74 days for which images were available. However, daily prey count became uncertain in the final 20 days of the study as the growing eaglets began to move into the branches around the nest, outside the view of the camera. The majority of prey items caught were riverine fish. Suckers (*Moxostoma* spp.) represented the majority of the fish caught during the study, but 9 different fish taxa were provisioned to the eaglets. Smaller numbers of birds and mammals were also caught, as well as several turtles. Mammals (4 taxa) and birds (5 taxa) diminished in frequency as the study progressed, which may have been due to increased foliage during the spring that decreased hunting success for these prey types.

HUFFMAN, ALLISON (28)

Novel regulatory functions of ESX-1 substrates in pathogenic mycobacteria

Research by Allison Huffman under the supervision of Alexandra Chirakos

Pathogenic mycobacteria such as *Mycobacterium tuberculosis* are a significant threat to global health. The ESX-1 secretion system is essential for the pathogenesis of mycobacteria. Our lab previously demonstrated that the levels of virulence factors secreted by the ESX-1 system are regulated by the WhiB6 transcription factor in response to the status of the ESX-1 system. The goal of our research is to determine the mechanism of transcriptional regulation of *whiB6* gene expression by ESX-1 substrates. We hypothesized that ESX-1 substrates function to regulate the *whiB6* gene expression. To determine the role of ESX-1 substrates in negative regulation of the WhiB6 transcription factor, we monitored the impact that overexpression of ESX-1 substrates had on WhiB6 protein production. We found that overexpression of *espE,* but no other substrates, reduced the levels of WhiB6 protein. Additionally, deletion of the *espE* genes resulted in an accumulation of ESX-1 substrates in the cytosol, a hallmark of missing negative regulators. Additionally, WhiB6 is significantly upregulated in the *ΔespE M. marinum* strain. We also conducted beta galactosidase assays to test the impact of overexpression of substrates on the *whiB6* promoter in a strain expressing a *lacZ* fusion to the *whiB6* promoter. Together our findings suggest that overexpression of *espE* is sufficient to negatively regulate *whiB6* gene expression. Current work is aimed at developing strains to help determine the mechanism of EspE in regulation of the ESX-1 system.

HUFFMAN, WILLIAM (29)

Gas-phase Enrichment of Protein Termini by Differential-suppression Labeling Proteomics (DSLP)

William Huffman[1], Matthew M. Champion[1,2,3,4] Department of Chemistry and Biochemisty, Advanced Diagnostics and Therapeutics, Eck Institute for Global Health, Boler-Pars Center For Rare and Neglected Disease. University of Notre Dame, Notre Dame, IN 46556.

Proteins represent the terminal step in the central dogma. Proteins perform virtually all cellular functions, and are dynamically regulated in expression, stability, localization and activity. Proteins are polymers comprised of 20 natural amino acids and typically have an amino (N) and carboxy (C) terminus. The composition of the N-terminus is especially important, and can direct the protein to a location in the cell, determine the rate of degradation of the protein and other potential roles in the cell. Alterations to the amino acids at the N-terminus can have serious effects on an organism or pathogens ability to effect disease. Protein termini represent just a small fraction of a total protein and therefore are difficult to study by traditional proteomics which relies on breaking proteins into peptides prior to analysis. A typical protein has just one terminus, but will produce >50 non-terminal fragments. Here we have developed multiple strategies to directly enrich protein termini from protease-digested cell lysates directly in a mass spectrometer. This obviates the need to perform any biochemical isolation, instead developing novel chemical properties of *neo*-terminal peptides to alter their detection efficiency. We synthesized and utilize reagents with N-terminal specificity which converts internal peptides to anionic sulfonic acids, which causes them to ionize less efficiently on the mass spectrometer. The solutions were tested and analyzed by LC-MS, giving a suppression ratio between 10:1 and 5:1. The labeled peptide had poor retention on reverse-phase chromatography and ionization properties which suggest a dual mechanism for enrichment, both chromatographic and gas-phase. The process for enrichment of whole proteomes is progressing.

KALATHOOR, JACOB (30)

Analysis of *ptf1a:GFP* Expression in the Adult Regenerating Zebrafish Retina

Jacob Kalathoor, Manuela Lahne, David R. Hyde

Department of Biological Sciences, Center for Zebrafish Research, and Center for Stem Cells and Regenerative Medicine, University of Notre Dame, Notre Dame, IN 46556

170 million people worldwide suffer from various retinal diseases that cause vision loss and eventually blindness. While humans lack the capacity to regenerate lost retinal cells, adult zebrafish rapidly regenerate retinal cells lost upon damage. Light-damage-induced photoreceptor death triggers Müller glia cell dedifferentiation and their cell cycle reentry. Dividing Müller glial cells produce neuronal progenitor cells (NPCs), which continue to proliferate and eventually differentiate into the lost cell types. Interestingly, other neuronal cell types, such as amacrine cells, are also generated although they were not lost following light-damage. In agreement, a subset of proliferating NPCs upregulate *ptf1a:GFP,* which identifies cells committing to an amacrine and horizontal cell fate. The number of arising *ptf1a:GFP*-positive cells is far larger than the previously reported number of generated amacrine cells, which raises the question whether both proliferating cells and existing amacrine cells increase *ptf1a:GFP* expression. To identify whether *ptf1a:GFP*-positive cells at 96 hLT arose from proliferating cells, EdU was intraperitoneally injected into light-damaged *Tg[ptf1a:eGFP]* zebrafish every 12 hours beginning at 24hLT until 84 hLT. At 96 hLT, *ptf1a:GFP*-positive cells were observed in the inner (INL) and outer nuclear layer (ONL) and a subset of these co-labeled with EdU. While many *ptf1a:GFP*-positive cells in the INL expressed the amacrine cell marker HuC/D, co-labeling of *ptf1a:GFP* and HuC/D was rarely observed in the ONL. The latter may suggest that these ONL-based *ptf1a:GFP*-positive cells committed to the horizontal cell fate. In agreement, several *ptf1a:GFP*-positive cells elongated along the horizontal cell layer and extended processes from their cell bodies towards the outer plexiform layer. Having observed a large number of *ptf1a:GFP*-positive cells at 96 hLT, we are currently investigating whether similar numbers of HuC/D and EdU double-positive amacrine cells are present at 96 hLT and 7 days of recovery.

KAZA, TERESA (ORAL PRESENTATION)

The efficacy of using trans-splicing group I introns to suppress HIV

Advisor: Malcolm Fraser, Dept. of Biological Sciences, University of Notre Dame

Current treatment models for HIV rely on Highly Active Antiretroviral Therapy (HAART), which, although it can extend the lives of patients, is unable to completely clear the patient of the virus. Group I Introns represent a potential form of gene therapy which could be used as a novel form of antiviral treatment. In this project, we assessed the efficacy of the 128/128L group I introns, engineered to specifically target HIV RNA, by evaluating the induction of apoptosis in HIV infected CEM A cells expressing the 128 or 128L group I introns and the suppression of viral titer. We found that the 128/128L expressing cells experienced a higher incidence of apoptosis when exposed to HIV and were able to suppress HIV titer by 2-3 logs.

KELLY, SEAN (ORAL PRESENTATION)

The p-Process: Using the Concept of Detailed Balance to Study Proton-rich Nucleosynthesis in Supernovae

Advisor: Anna Simon, Dept. of Physics, University of Notre Dame

The p-process, the nucleosynthesis process responsible for producing many proton-rich nuclei of atoms heavier than Iron (Fe), occurs in the Oxygen-rich layers of type II and Ia supernovae. During this process, seed s-process nuclei photo-disintegrate via (gamma, p) and (gamma, alpha) reactions producing proton-rich isotopes between selenium and mercury. In order to study this process, the principle of Detailed Balance for kinetic systems is utilized, allowing us to experiment with the inverse reactions: (p, gamma) and (alpha, gamma). HECTOR, or the High EfficienCy Total absOrption spectrometeR, was developed at the University of Notre Dame by Dr. Anna Simon for studying these processes. The NaI crystals in the detector allow us to use gamma-summing techniques to experimentally verify cross sections for these reactions, so that better understanding of the production of p-nuclei can be achieved. In this work, I will present on the data collected with HECTOR in the Notre Dame NSL and the methods used to analyze the data and calculate cross sections. Specifically, I will present on obtaining 90Zr(a,g)94Mo reaction cross sections at beam energies of 7.5 MeV-11.3 MeV. Results are in agreement with NON-SMOKER simulations, a group working on the same cross sections at the NSCL (Michigan State University), and graduate students in my research group.

KEMPF, HALEY (31)

The Role of Delta Ligands in Notch Signaling Pathway during Retinal Regeneration in Zebrafish

Advisor: David Hyde, Dept. of Biological Sciences, University of Notre Dame

The Adult zebrafish possesses the ability to regenerate the majority of its tissue and organ systems following damage, including the brain, spinal cord, and retina (Bernardos et al., 2007; Chapouton et al., 2010; Dias et al., 2012; Kroehne et al., 2011; Sean C. Kassen et al., 2007; Vihtelic & Hyde, 2000). Specifically, the regenerative response is largely mediated by Muller glia cells that undergo an asymmetrical division and produce a population of transient amplifying neural progenitor cells (NPCs) that migrate to the site of cell damage and differentiate into the lost neuronal cell types.(Fimbel et al. 2007; C. M. Nelson et al. 2013; Ramachandran et al., 2010; Vihtelic and Hyde 2000; Yurco and Cameron 2007). One model of regulation of muller glia cells involves a pathway known as Notch. This is initiated by the binding of delta ligands, followed by ubiquitination, and cleavage of the intracellular domain (ICD) of the receptor by enzyme complex, γ-secretase. This cleavage triggers the intracellular domain (ICD) to advance towards the nucleolus where it initiates the transcription of specific proteins from target genes (Conner et al., 2014). Chapouton et al., showed that an inhibition of Notch is associated with an increase in neurogenesis (2010). This summer, my project explored the behavior of three Delta-like (DLL) ligands DLL1, DLL3, and DLL 4 on muller glial proliferation. After recapitulating the morpholino knockdowns collected by Hobgood & Hyde, I confirmed that knocking down ligands A, C, and D decreased proliferation, while knocking down ligand B increased proliferation. Based on these results, I conducted a morpholino knockdown for each of these ligands at 36 hr and 72 hr light treatment in the gfap: GFP x Tp1 : mCherry line. This line was chosen because mCherry is expressed in cells where notch signaling is active. As expected, this experiment demonstrated limited proliferation at 32 hrs LT after knocking down ligand A, D, and LL4, and an increased proliferation after knocking down ligand B. At 72, hr LT, there was an increase in neuroprogenitor cells which represented recovery following light damage. Finally, I began genotyping to acquire a mutant line for delta A, C, and D with the intention of confirming the results of the morpholino knockdowns.

KIM, SANG WOO (RYAN) (ORAL PRESENTATION)

Optimization of High-Energy Photon Identification at the LHC

Ryan Kim[1], Livia Soffi [2], Francesco Micheli [3], Riccardo Paramatti [4], Colin Jessop [1]
[1] University of Notre Dame, [2] Cornell University, [3] ETH Zurich, [4] University of Rome Sapienza

Located at the border of France and Switzerland, the Large Hadron Collider (LHC) is an underground circular particle accelerator with a 17-mile circumference. It accelerates beams of protons to nearly the speed of light and collides them at one of the four detectors located throughout the accelerator. These detectors, including the Compact Muon Solenoid (CMS) detector, capture the sprays of subatomic particles that ensue from the initial collisions of protons. The CMS Collaboration designed, built, and operates the CMS detector and analyzes data from it with the goal of learning more about the fundamental building blocks of matter that make up our universe.

One type of a particle that is detected by the CMS detector is a photon. Low-energy photons are common in the detector with many known physical processes associated with them, and a highly-accurate identification method (ID) exists for them. However, high-energy photons are much rarer, and though a high-energy photon ID has previously been developed for a specific kind of physical analysis, that ID is not appropriate for more general usage in multiple analyses. High-energy photons could be key to new physics if observed in excess with the right physical processes, so the goal of this project is to develop an improved and more general ID for them.

A selection-based approach is used for the ID, where several variables characteristic of high-energy photons are taken and given a range of cuts. The optimal cut ranges provide the best signal (high-energy photons) to background (non-signal events that can mimic the signal) ratios. Monte Carlo simulations are used to develop the ID since every particle is known in simulations and it is feasible to evaluate how well the ID performs. Once satisfactory levels of performance are reached with simulations, the ID can be applied to data from the detector.

KOENIG, JENNA (32)

Functional Screen Identifies Triple-Negative Breast Cancer Vulnerability Driven by Death Effector Domain-Containing Protein

Yingjia Ni, Keon R. Schmidt, Barnes A. Werner, Jenna K. Koenig, Ian H. Guldner, Patricia M. Schnepp, Xuejuan Tan, Lan Jiang, Misha Host, Longhua Sun, Erin N. Howe, Junmin Wu, Laurie E. Littlepage, Harikrishnaand Nakshatri, and Siyuan Zhang

Triple-negative breast cancer (TNBC) has a poor prognosis. There is no FDA approved targeted therapy for TNBC patients due to the lack of well-defined therapeutic sensitivity biomarkers for tumor-specific vulnerabilities conferred by dysregulated TNBC genome. Although basal-like TNBC tumors express one of the most important therapeutic targets, epidermal growth factor receptor (EGFR), the results of clinical trials using anti-EGFR therapy towards TNBC have been disappointing. To discover the potential synthetic lethal interactions under the context of EGFR inhibition, we conducted a genome-wide pooled barcoded shRNA targeting 5,403 human genes using a TNBC cell line (HCC1806). We identified the Death Effector Domain-containing protein (DEDD), which is up-regulated in >70% clinical TNBC tumors, is an essential driver for the survival of TNBC when EGFR signaling is abrogated. Mechanistically, cytosolic DEDD, not the nuclear DEDD, facilitates mitogen-independent G1-S transition through a direct interaction with RB, leading to its proteasome degradation. Moreover, the interaction between cytosolic DEDD and Heat Shock 70 kDa Protein 8 (HSC70) enhances HSC70-mediated RB-independent G1-S transition. We further demonstrated that pharmacological inhibition of G1-S regulator CDK4/6 impairs DEDD-driven cell cycle transition and sensitizes TNBCs to EGFR inhibitor in both TNBC cell lines and TNBC PDX, regardless of RB status.

KOH, SOJUNG (33)

Estimation for a predictive function for MMR vaccination behavior as a function of year and age

Sojung Koh, Kenneth Soda, Alex Perkins

University of Notre Dame

Measles is a highly contagious viral disease that can potentially cause pneumonia, encephalitis, and even death. Measles transmission is currently on the rise globally is recently facing situations of lower rates of vaccination. If such low rates persist, the increasing number of unvaccinated individuals will lead to worsening outbreaks and could possibly even lead to the re-establishment of endemic measles if vaccine coverage deteriorates to a large enough extent. We developed a model designed to predict the probability an individual has received at least one dose of MMR vaccine as a function to their age, the current year, and their socioeconomic characteristics. We formulated this model as a bivariate hazard function in two continuous dimensions: year and age. We considered two alternative formulations of the cumulative hazard function that have different implications for how hazards are shared across children surveyed at different ages in different years. Refinements of this model that depend on socioeconomic factors were explored, with particular features used in the model being chosen on the basis of model selection with Akaike information criterion. Characteristics including race, maternal education, maternal marital status, family income, poverty, and sex were considered. The model was fitted to three datasets published by the Centers for Disease Control and Prevention that reflect surveys carried out in a subset of the population for infants, toddlers, and teenagers, mostly at the state level, and stratified as a function of these demographic characteristics. There was a strongly decreasing hazard of vaccination with age under all versions of the model that we considered. There was an increasing effect of year, although this slowly began to decrease in recent years. Several socioeconomic factors variables had significant effects. The model we developed has implications for estimation of vaccination coverage for measles and helps extract nuanced information about vaccination behavior from publicly available data sources.

KORAN, REINA (34)

Determining the role of Tnf receptor 1a in zebrafish retinal regeneration

Advisor: David Hyde, Dept. of Biological Sciences, University of Notre Dame

The zebrafish retina is similar to the mammalian retina in organization and complexity, however zebrafish have the ability to regenerate the retina after damage. A requirement for zebrafish retinal regeneration is TNFα, a proinflammatory cytokine secreted by the dying retinal neurons. I have hypothesized that the TNF receptor Tnfr1a is also necessary for regeneration. In order to investigate the role of Tnfr1a, I performed immunofluorescence assays with an antibody against zebrafish Tnfr1a and examined proliferation in the *tnfrsf1a*^{sa15813} mutant zebrafish. The immunofluorescence assay was optimized by testing various fixation conditions, antigen retrieval methods, and antibody concentrations. The optimal combination for the Tnfr1a antibody was 4% paraformaldehyde/5% sucrose fixative with a 1% SDS antigen retrieval incubation and 1:50 antibody dilution. The antibody signal can be detected in the inner nuclear layer of the retina and appears to outline the cell bodies and some processes of Müller glia. The Tnfr1a antibody signal was not detected in the homozygous *tnfrsf1a*^{sa15813} mutant. In order to test whether Tnfr1a is necessary for retinal regeneration, I performed a light treatment time course on wild type, heterozygous, and homozygous *tnfrsf1a*^{sa15813} fish that were between six and twelve months old. Retinal sections from 36 and 72 h light-treated eyes were immunostained with DAPI to identify nuclei and PCNA to identify proliferating cells. PCNA-positive proliferating Müller glia were detected following light damage in the *tnfrsf1a*$^{-/-}$ retina. This may indicate that *tnfrsf1a*$^{-/-}$ fish develop a mechanism to compensate for loss of Tnfr1a in the regeneration process by overcoming the lack of the functional receptor. Alternatively, it is possible that the mutation did not have the expected truncation effect on Tnfr1a. Further studies using a morpholino oligonucleotide to knockdown Tnfr1a prior to light treatment will help to determine whether compensation is playing a role in the *tnfrsf1a*^{sa15813} mutant.

KOSZUTA, PETER (35)

Detection and Functionalization of Non-Standard Carbenes

Advisor: Jon Camden, Dept. of Chemistry, University of Notre Dame

N-heterocyclic carbenes (NHCs) and non-standard carbenes are structures of relative stability, and can be functionalized into more diverse compounds. In theory, these can be grown into very large and complex molecules, and are stabilized on FONs surfaces. Analysis and detection of carbenes was performed on novel non-standard carbenes using SERS and Raman spectroscopy. Unique spectra were obtained of many target compounds which were prepared and synthesized both in lab and commercially. The spectra obtained and processed aid in the understanding of carbenes. Preparation and deposition of samples were refined. Non-standard carbenes are a developing area of interest, with potential to aid in analysis and research on novel compounds. Detection and analysis are vital to identifying and realizing the changes and potential of these molecules and methods.

KURKOWSKI, MICHAEL (ORAL PRESENTATION)

Nuclear Astrophysics Calculations Performed by the LANCE of St. George

Advisor: Manoel Couder, Dept. of Physics, University of Notre Dame

To understand aspects of stars and stellar properties, a thorough study of the nuclear fusion reactions that power them is necessary. These reactions can be reproduced in the Nuclear Science Laboratory (NSL) using the Sta. Ana accelerator and the St. George recoil separator. This work focuses on one facet of the reaction study, specifically the prediction of the the charge state fraction of ions as they pass through a target. ETACHA is a program that performs this calculation for a given beam charge state and returns the final charge state without taking into account other interactions with the target. In this work, attention is drawn to a partner program LANCE, which runs ETACHA and processes the output data.

LABB, LAURA (36)

Artificial Light at Night Promotes Blood Feeding of Ae. Aegypti Mosquitoes

Advisor: Samuel Rund, Dept. of Biological Sciences, University of Notre Dame
Giles Duffield, Dept. of Biological Sciences

As light pollution continues to plague both developed and developing countries alike, the implications of light pollution on the biting pattern of the normally diurnal mosquito species *Ae. aegypti* must be considered. The *Ae. aegypti* mosquito is the vector of many tropical diseases including dengue, yellow fever, chikungunya, and Zika virus, and thus increased biting elevates risk for disease transmission to affected communities. We suspected that artificial light at night would increase nocturnal biting of *Ae. aegypti* compared to those not in the presence of light pollution. Mosquitoes were raised in a 12:12 light dark schedule to acclimate to normal conditions, then manipulated to expose an experimental group to 30 minutes of dim light prior to ZT18 while a control group received no such treatment. An additional group was offered a blood feed at ZT10 to establish a baseline of biting frequencies for mosquitoes during a typical biting period. A higher percent of mosquitoes from the experimental group exposed to artificial light blood fed at ZT18, suggesting that the presence of light increases nocturnal blood feeding. The conclusions drawn from this study highlight a significant epidemiological effect of artificial light on the nocturnal biting frequencies of diurnal species and human risk of disease transmission associated with increased light pollution globally.

LEE, JESSICA (37)

Investigation of Permethrin Resistance in *Aedes aegypti* Mosquitoes

Advisor: Nicole Achee, Dept. of Biological Sciences, University of Notre Dame

The *Aedes aegypti* mosquito is a primary vector of many arboviruses of global health burden that include dengue, chikungunya, Zika , and yellow fever viruses, among others. The control of these mosquitoes, through chemical methods such as indoor thermal fogging, is a key element in reducing human cases. This project will generate data regarding the insecticide resistance status of a strain of *Ae. aegypti fr*om Belize, Central America. Populations of non-fed, female *Ae. aegypti* mosquitoes will be exposed to the diagnostic doses of permethrin, a pyrethroid chemical commonly used for dengue control, using the Centers for Disease Control and Prevention (CDC) bottle bioassay methodology, and time-mortality data will be recorded following permethrin exposure. The findings of this research will allow for the detection of potential permethrin resistance in the population. Information derived from this CDC bottle bioassay is intended to provide initial evidence of permethrin effectiveness as part of a broader Belize Ministry of Health insecticide resistance monitoring program.

LIPA, DANIEL (38)

The Effect of Hydrogen Peroxide Gas from an Atmospheric Pressure Plasma Jet on a DNA sample

Advisor: Sylwia Ptasinska, Dept. of Physics, University of Notre Dame

Plasma medicine is an emerging field that has been shown to treat burns and other forms of trauma using open air atmospheric pressure plasma jets (APPJ). In order to increase the clinical performance of the jet, the reactive species must also be increased. One possible way of increasing the reactive oxygen species of the plasma is to have hydrogen peroxide vapor in the feed gas of the APPJ. However, it was found that the reactive oxygen species are not very reactive to aqueous DNA. In this work, it will be determined if there is any hydrogen peroxide in the DNA sample. Aqueous DNA was irradiated by the plasma jet with different time levels of irradiation. The hydrogen peroxide was detected by Amplex Red and quantified using a hydrogen peroxide standard curve. The results of this experiment show that very little hydrogen peroxide was found in the actual contents of the aqueous irradiated DNA, which confirms that the reactive oxygen species that are formed in the plasma jet when hydrogen peroxide vapor is in the feed gas is not very reactive to the aqueous DNA.

LIU, YUTONG (ORAL PRESENTATION)

7-hydroxystaurosporine (UCN-01) Demonstrate Broad-Spectrum Antiviral Activity Against Lipid-Enveloped Viruses Through Membrane Phosphatidylserine Modulation Action

Yutong Liu[1], Mark Fraser[2], Arwa Mohammad[1], Malcolm Fraser[1]
1.Department of Biological Sciences, University of Notre Dame, 2.Intergrated Biomedical Sciences, University of Notre Dame

Lipid-enveloped viruses such as the re-emerging Chikungunya virus and the emerging Zika virus present a significantly rising threat to global health. In 2015 693,489 suspected cases of Chikungunya were reported in the Americas, while over 80 countries have signs of Zika transmission. While work on immunization and specific drug development is ongoing, there is a lack of a broad spectrum antiviral strategy against lipid-enveloped viruses. Previous reports have described UCN-01 to have membrane phosphatidylserine (PS) modulating activity and identified TIM (therefore PS) dependent viral entry by lipid-enveloped viruses through viral apoptotic mimicry. This led to the hypothesis that UCN-01 can prevent viral entry and infection of host cells by decreasing the PS concentration and thus serve as a broad-spectrum antiviral for lipid-enveloped viruses. This is further backed by preliminary data that suggest UCN-01 can successfully inhibit HIV up to 2 logs and Ebola over 1 log in-vitro. This study investigates UCN-01's antiviral activity for Chikungunya and Zika viruses. Vero and Vero 81 cells were treated with varying doses of UCN-01 and infected with Chikungunya and Zika Virus, respectively. TCID-50 assays were performed on cellular supernatants and the Reed and Muench method was used to calculate the viral load. Chikungunya showed full inhibition at a MOI of 10^{-4} with a 100nM treatment of UCN-01, but no significant reduction of viral load was observed at a MOI of 10^{-3} with any level of treatment. For Zika, a 100 nM treatment of UCN-01 resulted in up to 2 logs of inhibition at a MOI of 1. In conclusion, UCN-01 is able to inhibit Chikungunya virus in-vitro at low levels of infectious and Zika virus even at high levels of infection. Future research should focus on testing UCN-01 on other lipid-enveloped viruses and in animal models to further validate it as a antiviral candidate.

LOHR, NICHOLAS (ORAL PRESENTATION)

Approximating Riemann Mappings by Circle Packings

Advisor: Jeffrey Diller, Dept. of Mathematics, University of Notre Dame

One of the major results in complex analysis is the Riemann mapping theorem, which states that every nonempty, proper, open, and simply connected subset $\Omega \subset \mathbb{C}$ is conformally equivalent to the unit disk. However, like many existence theorems, the Riemann mapping theorem does not show how to obtain this map from Ω. To remedy this, William Thurston, at the Bieberbach conference in 1985, conjectured that circle packings, an arrangement of circles inside a given boundary such that no two overlap and all of them are mutually tangent, can be used to describe a discrete counterpart to the Riemann mapping theorem, namely, mapping circle packings inside Ω to circle packings inside the unit disk. We are interested in proving that these mappings converge to the biholomorphic mapping guaranteed by the theorem in the continuous limit and creating a program to demonstrate circle packings.

LOPEZ, EDWARD (39)

Spatial and temporal variation in nutrient availability drives biotic nutrient removal in agricultural streams and floodplains

Edward Lopez, Matt T. Trentman, Jennifer L. Tank

Ecological stoichiometry can inform our understanding of biogeochemical cycling in aquatic systems and its influences on associated microbial processes, such as microbial respiration and denitrification. Nutrient removal via biological processes is of specific interest in the agricultural Midwest, where maximizing nutrient removal from streams is one mechanism for alleviating eutrophication in downstream waterbodies. In order to determine the impacts of soil and sediment parameters on biological transformations in streams, we measured total nitrogen (N), carbon (C) and phosphorus (P) in floodplain soils and adjacent stream sediments. We analyzed samples collected across four seasons in three agricultural streams in northern Indiana. We predicted that there would be spatial variation in stoichiometric ratios associated with distinct soil properties at each site. Specifically, we predicted that sites dominated by clay would be limited in N and P availability due to low organic matter quantity. The frequency of floodplain inundation also plays a role in soil characteristics, as flooding promotes an exchange of nutrients. We predicted that more frequent and longer inundation in spring would increase relative nutrient availability due to the deposition of nutrients. We observed spatial variation in C:N and C:P ratios in both stream sediments and floodplain soils. However, we only observed seasonal variation in C:P ratios in floodplain soils, which primarily was lowest in spring indicating decreased P limitation. Microbial respiration in floodplain soils was positively correlated with both total C and N ($p<0.001$), and decreased with increasing C:N ($p<0.001$) indicating the limitation of microbial respiration at higher C:N ratios. While we did not measure denitrification, lower C:N ratios in floodplains at two of the three sites likely results in more nutrient removal via denitrification. Overall, we found that spatial variability of the nutrient stoichiometry in soils and sediments likely impacts the degree of biotic nutrient removal.

MALIBORSKI, EMILIA (40)

The Effect of Synchrony on Six-Month-Old Infants' Object Encoding

Dr. Jill Lany, Ariel Aguero, Emilia Maliborski
Department of Psychology, University of Notre Dame, Notre Dame, United States

Words can affect how infants attend to and learn about objects, and parents often couple an object's movement with its name when teaching infants. Temporal synchrony, or the redundancy of a stimulus across two or more sensory systems, may direct infants' attention and emphasize the amodal properties of a stimulus[1]. The purpose of this study is to determine whether the synchrony parents create when labeling objects helps infants to encode those objects. Six-month-old infants watched a video that introduced them to images of novel objects and auditory labels for those objects. The object moved synchronously or asynchronously with its label, or remained stationary (static). To test infants' learning, their looking times to the now familiar object against a second novel object in silence were compared. There were three different tests to determine how well and which features of the familiarized object were encoded: a completely different novel object (Easy), a novel object of same shape but different color (Color Different), and a novel object of different shape but same color (Shape Different). The results demonstrate that infants who were familiarized with asynchronous or static object movement performed poorly across all trials; while these infants showed a slight preference for the familiar object in the Easy test, they looked at chance in the Color Different and Shape Different trials. Infants familiarized with synchronous movement demonstrated object discrimination across all trials; they showed a preference for the object with the same shape as the familiarized object in the Easy and Shape Different tests, and for the object of the same shape but different color in the Color Different test. The results suggest that auditory-visual synchrony influences six-month-old infants' ability to encode both shapes and colors of objects, and provides support for the helpful effects of synchrony in infant learning and language development.

Reference

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MARFOWAA, GIFTY (42)

Intraperitoneal Mechanobiology in Ovarian Cancer: A Biomimetic Approach

Leigh Campbell[1], Brooke Kowalski[1], Gifty Marfowaa[1], Dung Trung Nguyen[3], Gozde Basara[3], Tyvette Hilliard[1,2], Yueying Liu[1,2], Pinar Zorlutuna[3], M. Sharon Stack[1,2]
[1]Harper Cancer Research Institute,
[2]Department of Chemistry and Biochemistry, University of Notre Dame, IN
[3]Department of Aerospace and Mechanical Engineering, University of Notre Dame, IN

Ovarian Cancer (OvCa) is the fifth leading cause of cancer-related mortalities in women. OvCa is typically detected and diagnosed after extensive intraperitoneal (IP) metastases, contributing to 5-year survival rates that have not substantially improved in over 30 years. Unlike other cancers, OvCa metastasis occurs when tumor cells detach from the primary tumor, permeate throughout the peritoneal cavity in the peritoneal fluid, adhere to the mesothelial layer of peritoneal tissues and invade the collagen-rich submesothelial matrix. The peritoneum is a tissue membrane under longitudinal tensile stress which fluctuates in response to changes in IP fluid volume. Normal intraperitoneal pressure (IPP) is ~5 mmHg, but averages 22.1 mmHg in women with OvCa and tense ascites. Previous research indicates that high IPP is associated with increased abdominal metastasis in a murine OvCa model. Our lab previously found that increased IPP results in increased tissue stiffening. Moreover, nano-indentation, a technique used to test the mechanical properties of materials, also demonstrated an increase in tissue stiffness in peritoneum tissues from aged versus young mice. Aged tissue exhibits an elevated melting point for collagen, indicating increased collagen crosslinking, resulting in stiffer tissue. Finally, it is also well known that aged collagen tends to exhibit decreased fiber density and sinusiodosity along with increased fiber alignment - a set of characteristics known as the “tumor-associated collagen signature” (TACS). TACS is an indicator of poor prognosis in breast cancer, which suggests that aged collagen may play a role in OvCa metastasis. Epidemiologic data suggests that age is a significant risk factor for OvCa incidence. Nevertheless, there have been few investigations of age-related changes in peritoneal tissues and their impact on OvCa metastasis. The purpose of this study is to further examine how age-induced changes in peritoneum physical properties, specifically tissue rigidity, affect OvCa cell adhesion, spreading, and gene expression using an innovative biomimetic stiffened gel model. We report that two human OvCa cell lines have increased adhesion and spreading on the stiffened gels, which are both key indicators of metastatic process. Taken together, these findings suggest that aged peritoneum stiffening may play a role in metastatic susceptibility. Future assessment of gene expression between OvCa cells on stiffened gels is needed to identify differentially regulated genes that enable OvCa adhesion.

MATTHEWS, BRADEN (41)

Selective Photothermal Heating with Near-Infrared Croconaine Rotaxanes

Hannah H. McGarraugh, Wenqi Liu, Braden Matthews, and Bradley D. Smith
Smith Lab, University of Notre Dame, Notre Dame, United States

There is increasing interest in developing methods of generating heat in nanoscale environments. The most common approach uses the photothermal effect, namely the absorption of laser light by molecules or particles that convert this energy into heat. An area of interest for light absorption is the near-infrared (NIR) window, due to the minimal background signal, sharp probe signals, and increased depth penetration in *in vivo* applications. There are very few dyes that absorb strongly in the NIR region and of these dye families, croconaines remain a relatively unexplored group. We have previously shown that croconaines can be converted to rotaxane structures which exhibit sharp absorption bands, even under conditions that aggregate the molecules. Here, we will show previously reported thiophene croconaine dye **C1** and its newly extended thienothiophene counterpart **C2** as well as their relative rotaxanes **1** and **2**. These rotaxanes have distinct and non-overlapping absorbance bands at 824 nm and 984 nm, which can be utilized for multiplex heating. Photothermal heating experiments showed that solutions of rotaxanes 1 and 2 are selectively heated with 830 nm and 980 nm laser diodes, respectively. This can be utilized for various applications of photothermolysis including photothermal cancer therapy (PPT), photoacoustic imaging (PAI), drug delivery, tissue repair, photothermal reactions, and polymer welding.

Keywords: photothermal therapy, near-infrared probes, croconaine dye, selective heating

MATTHEWS, LAURA (43)

Physiological Effects of Microplastics on Yellow Perch (*Perca flavescens*)

Authors: Laura M. Matthews, Whitney M. Conard, Gary A. Lamberti

Microplastics are plastic particles <5 mm in diameter that are now ubiquitous in aquatic ecosystems and do not readily degrade. Because microplastics are ingested by animals and can bioaccumulate in aquatic food webs, they may directly impact physiological function. Unfortunately, the physiological impacts of microplastics have received little research attention but are pertinent to prioritizing the regulation of microplastics in the environment. This research examined how yellow perch (*Perca flavescens*) physiology can be affected by microplastic ingestion. A 40-day feeding experiment was conducted with three treatment groups: (1) normal diet of food pellets (100%), (2) 90% normal diet, and (3) 90% normal diet injected with 10% sterile microplastics. These treatments were also contrasted with fish that refused to eat (0% normal diet). We found no significant differences among the treatment groups for changes in fish length, mass, condition, or respiration rates. We observed that microplastics passed through the intestines as undigested material without accumulation. These results suggest that low levels of microplastic ingestion have little effect on fish health and growth. However, the impacts of microplastics may be more subtle or complex than this study could measure. Future research should explore chemical contaminants adsorbed by microplastics.

MCCLINTOCK, STEPHANIE (44)

APC loss alters DNA damage repair in breast cancer cells

Stephanie McClintock[1,2], Casey Stefanski[1,2], Kaitlyn Keffler[1,2], and Jenifer R. Prosperi[1,2,3]
[1]*Department of Biological Sciences, University of Notre Dame, Notre Dame, Indiana*
[2]*Harper Cancer Research Institute, South Bend, Indiana*
[3]*Department of Biochemistry and Molecular Biology, Indiana University School of Medicine-South Bend, South Bend, Indiana*

Breast cancer is the second leading cause of cancer deaths in U.S. women. Many of these deaths have been attributed to the development of chemotherapeutic resistance. Thus, understanding chemoresistance will help develop novel approaches to combat breast cancer. The *Adenomatous Polyposis Coli* (*APC*) tumor suppressor is silenced or mutated in up to 70% of sporadic breast cancer; however, the effects of APC loss on chemoresistance has not been elucidated. Using the $Apc^{Min/+}$ mouse crossed to the Polyoma middle T antigen (PyMT) transgenic model, we previously showed that APC loss decreased doxorubicin-induced apoptosis and increased STAT3 activation causing increased multidrug resistance protein 1 (MDR1) expression. Here, we hypothesize that APC loss increases doxorubicin efflux and increases DNA damage repair. First, we show that APC loss increased MDR1 activity as measured by calcein flux. To determine whether MDR1 inhibition restores doxorubicin-induced DNA damage, a combination treatment of doxorubicin and MDR1 inhibitor, Valspodar, was able to restore doxorubicin sensitivity in MMTV-PyMT;$Apc^{Min/+}$ cells compared to control. In addition, we have shown a decrease of γH2AX, a marker of damaged DNA, in MMTV-PyMT;$Apc^{Min/+}$ cells treated with doxorubicin suggesting a damage decrease due to increased drug efflux via MDR1 or to increased DNA damage repair. To test if this decrease in DNA damage is concentration dependent, we treated with bleomycin which causes DNA damage, but it is not affected by MDR1. Future studies will measure DNA damage repair pathway efficiency via reporter plasmids and measure downstream signaling of yH2AX. Through understanding of the role of APC in DNA damage repair, we can ascertain combination therapies to overcome chemoresistance.

MCGUIRE, PATRICK (45)

Automation of Lead Testing

Advisor: Graham Peaslee, Dept. of Physics, University of Notre Dame

A 2016 Reuters article (https://www.reuters.com/investigates/special-report/usa-lead-testing/) found that the city of South Bend is experiencing a lead poisoning crisis on a scale larger than that of Flint, Michigan, whose lead crisis has made national headlines since 2014. The year the issue in South Bend became widely known, the Notre Dame Lead Innovation Team (LIT) began testing local homes in order to assess exactly where in homes there lies the greatest risk for lead exposure, and investigate which neighborhoods were most at risk. This study involved visiting homes, and delivering personalized reports to homeowners noting which parts of the home were at risk, and instructions describing how the lead can be abated, or risk of exposure reduced. This process, unfortunately, is inefficient. As a result, at the project's inception, very few homes were tested. In order to provide assistance to more people, the team has partnered with local middle schools, where students receive kits to obtain samples from their homes that are then sent to our laboratory for analysis. In order to process all of these samples in a timely fashion, we have been building an automated testing system involving an x-ray fluorescence (XRF) machine and conveyor belt operated by an Arduino microcontroller. Being able to run these samples without human intervention is an essential step in the expansion of our current operation, allowing us to collect more data that can help us better understand the threat of lead poisoning, as well as provide assistance to those afflicted by the lead crisis.

MEHLMANN, KRISTIN (46)

Characterization of the Plants Consumed by Long-tailed Macaques (*Macaca fascicularis*) in Bali, Indonesia

University of Notre Dame Department of Biological Sciences
Kristin Mehlmann, Benjamin Gombash, and Hope Hollocher

Animal diets provide important context for analyzing communities of parasites and microbes, both individually and at the population level, and access to anthropogenic food can influence these communities. Humans and long-tailed macaques live in close proximity on the island of Bali, Indonesia, and have done so for centuries. Consequently, Balinese macaques consume a diverse diet which includes a wide variety of plant items from both anthropogenic and non-anthropogenic sources that can range from sweet potatoes provisioned to them by park officials to plants they forage in the wild. In order to understand more fully the breadth of the macaque diet in Bali and its human influences, fecal samples were collected from twelve macaque populations across the island that vary markedly in their levels of anthropogenic contact. We then employed 18S rRNA gene metabarcoding to identify plant species, specifically embryophytes, present in those fecal samples. Next, we constructed a plant category database to evaluate each identified embryophyte's functional role(s) at the island level, focusing on anthropogenic categories, such as religious and ornamental plants that are used ubiquitously in Balinese temple offerings. This characterization will prove useful for answering future questions about our study system at both the island and population levels, more specifically the intra-island population differences in Bali and inter-island differences between Bali and other locations with macaque populations. These questions include exploring the complex relationships between diet and parasite community structures as well as diet and microbiome compositions, and how humans influence these relationships.

MILAC, LAUREN (47)

Loss of APC Mediates Doxorubicin Resistance Through Enhanced DNA Repair Pathways

Lauren Milac[1,2], Casey Stefanski[1,2], Kaitlyn Keffler[1,2], Stephanie McClintock[1,2], Jenifer Prosperi[1,2,3]

[1]College of Science, University of Notre Dame, Notre Dame, Indiana
[2]Harper Cancer Research Institute, Department of Biological Sciences, University of Notre Dame, Notre Dame, Indiana
[3]Department of Biochemistry and Molecular Biology, Indiana University School of Medicine-South Bend, South Bend, Indiana

DNA damage repair pathways greatly influence the response to chemotherapeutic drugs in cancer cells. Doxorubicin (DOX) is a common chemotherapy used in breast cancer that works by inducing DNA double stranded breaks (DSBs); however, an issue with chemotherapies such as DOX is the potential for resistance. It has been shown that the loss of the tumor suppressor Adenomatous Polyposis Coli (APC) can lead to reduced sensitivity to chemotherapy drugs, cisplatin, paclitaxel, and DOX. Previously we have shown that there is decreased DNA damage at 24 hours with DOX treatment in APC-deficient breast cancer cells. Since DSBs are repaired via non-homologous end joining repair (NHEJ) or homologous recombination (HR), the expression of the catalytic subunit of DNA repair protein, DNA-PK, was experimentally tested to see if APC loss increased the cancer cell's ability to repair DOX-induced DNA damage. We show that there is enhanced basal levels of the catalytic subunit of DNA-PK in MMTV-PyMT;$Apc^{Min/+}$ but no change between MMTV-PyMT;$Apc^{Min/+}$ and MMTV-PyMT;$Apc^{+/+}$ following drug treatment. We also measured the expression of the HR-directed kinases, ATM and ATR, and found that DOX-induced activation of ATM in MMTV-PyMT;$Apc^{+/+}$ cells but activation was absent in APC-deficient cells. Using the DNA repair inhibitors we found that the DNA-PK inhibitor (NU7441) or the ATM inhibitor (KU55933) in combination treatment with DOX restored DOX-mediated apoptosis in MMTV-PyMT;$Apc^{Min/+}$ cells compared to MMTV-PyMT;$Apc^{+/+}$ cells. Future studies will examine NHEJ and HR repair efficiency through reporter plasmids and *in vivo* work. In conclusion, our data show that inhibition of DNA-PK or ATM may be an effective approach to enhance the tumor killing effects of DOX in APC-deficient breast cancer.

MILLER, CASSANDRA (48)

Predictive modeling of time spent outside to inform vector-borne disease exposure

Cassandra Miller, Rachel Oidtman, Alex Perkins

As occurrences of vectors and associated vector-borne diseases in the United States continue to rise, there is a need to more accurately predict the risk of people contracting these diseases. The goal of this research is to model the amount of time that individuals spend outside and understand the impact this has on their risk of contracting such a vector-borne disease. The U.S. Bureau of Labor Statistics annually collects and makes available the American Time Use Survey data. In this survey, there is information regarding the time that respondents spend doing different activities along with demographic variables about the respondents. By analyzing the activities and determining the total time that respondents spent doing outdoor activities, statistical models were trained to predict the total time that a person spent outside based on their set of demographic variables. A variety of statistical models were fit using the demographic covariates to predict if an individual spent any time outside, and if so, how much time they spent outside. Preliminary results underscore the need to consider an ensemble modeling approach to predict time spent outside on a state level throughout the U.S. In the future, the goal is to apply the model to data with demographic variables available on the county-level to predict the time individuals spend outside on a finer scale and eventually use this as a predictor in modeling the risk of contracting vector-borne diseases.

MILLICAN, PATRICK (ORAL PRESENTATION)

Measuring the cross-section of cadmium-108 to constrain the p-process in type II supernovae

Advisor: Anna Simon, Dept. of Physics, University of Notre Dame

The means by which the p-nuclei, which are nuclides that are stable despite being neutron-poor, are synthesized is not fully understood in nuclear astrophysics. As a result, the attempts at modeling p-nuclei nucleosynthesis have resulted in theoretical abundances that differ from observed ones. The most likely nucleosynthesis of p-nuclei is the gamma-process: in core-collapse supernovae a flux of high-energy photons is thought to trigger the (γ, p), (γ, α), and (γ, n) photodisintegration reactions with heavier-than-iron isotopes produced during ordinary stellar burning. Once the surrounding medium cools, the resultant nuclei can beta-decay into stable p-nuclei. Accordingly, it is necessary to measure the cross-section for the reverse of (γ, p) and (γ, α) photodisintegration, namely (p, γ) and (α, γ) capture reactions. Cadmium-108, which has been identified as a p-nuclide of particular interest, is the focus of this presentation. Notre Dame's FN 10MV Tandem Accelerator was used to subject a ^{108}Cd target to bombardment by protons and HECTOR, a NaI(Tl) summing detector, was used to collect spectra that were later summed and calibrated using ROOT. The cross-section for the (p, γ) reaction for ^{108}Cd was measured at projectile lab-frame energies between 4.0 and 7.0 MeV. The results are in good agreement with previous results found in the literature for beam energies between 4.0 and 5.0 MeV; for beam energies between 5.0 and 7.0 MeV the results were always below the literature values and those predicted by the NON-SMOKER model by no more than a factor of 3.

MURPHY, MOLLY (ORAL PRESENTATION)

Role of microRNAs in the Putative Cancer Stem Cells for HNSCC

Advisor: Shi-Long Lu, Dept. of Otolaryngology, University of Colorado Anshutz Medical Campus

Although head and neck squamous cell carcinoma (HNSCC) accounts for approximately 4% of all cancer diagnoses in the U.S., recurrence and metastasis are common among patients, resulting in a relatively low 5-year survival rate below 50% that has not significantly improved over the past decades (Thomas *et al.*, Essentials of Genomic and Personalized Medicine 2010). Treatment plans typically consist of surgery, chemotherapy, and radiation; however, these do not adequately target putative cancer stem cells (CSCs), the alleged seeds for HNSCC recurrence, due to limited understanding of the mechanisms through which these cells survive and spread. Our lab has previously investigated signaling pathways in CSC's, specifically the PI3K pathway. Overexpression of the *PIK3CA* gene, which encodes the catalytic subunit of the phosphatidylinositol 3-kinase (PI3K) enzyme responsible for regulating cell growth, survival, motility, and metabolism, has been found to promote HNSCC progression by increasing epithelial-mesenchymal transition (EMT) and enriching the CSC phenotype (Du *et al.,* Oncogene 2016). While there are multiple molecular mechanisms responsible for CSC survival, our project is particularly interested in the role of microRNA's (miRNA), small nucleotides involved in gene regulation that target mRNA sequences and prevent protein translation. Using the CSC model, our lab has done a miRNA array to compare CSC's to non-CSC cancerous tumor cells; screening results showed differentiated expression of miRNA. We hypothesize that both the up-regulation of certain miRNA's inhibiting tumor suppressor proteins and the down-regulation of miRNA's inhibiting oncoproteins are responsible for maintaining CSC's survival; thus, interfering with the aberrant miRNA's and/or their downstream pathways may help reduce or eliminate the CSC population. The following specific aims are posed to test our hypothesis:

Aim 1: Validate differentiated expression of miRNA

We will isolate putative CSC populations from both mouse and human HNSCC through sphere-forming methods and flow cytometry. Then by quantitative PCR, we can evaluate potential expression correlation.

Aim 2: Characterization of each miRNA's role in maintaining the CSC state

Mimics or antimeres of miRNA's will modulate gene expression levels in CSC's. After cells are transfected with miRNA mimics, the maintenance of survival will be assessed by sphere-forming assays and/or CSC marker analysis.

Aim 3: Identify potential downstream targets and pathways of miRNA's that regulate CSC survival

Through bioinformatics and target scans, putative targets will be evaluated. The effects of knocking out certain genes expressed in CSC's will also be examined.

This goal of this project is to review the molecular mechanisms within CSC's, specifically the role of miRNA in regulating survival. This knowledge will likely translate into novel and improved therapeutic molecular targets, which can be exploited to eliminate or at least reduce CSC's. Identifying resulting potential treatments will hopefully yield fewer recurrences and metastases in clinical HNSCC patients.

MURTAGH, CAROLINE (ORAL PRESENTATION)

Connection of RAB8A and MED16 with implications on 5'-deoxy-5-fluorouridine response

Caroline Murtagh, Christy Lucas, Amy Stark

Treatment plans can be individualized to optimize cancer patient care by better understanding genetic influences on protein expression and drug response. This study aims to utilize genetic associations between protein levels and drug response to identify functional candidates for Capecitabine therapy optimization.Through unbiased whole-genome methods evaluating genetic variants, protein expression, and chemotherapy, we identified three SNPS localized to the short arm of chromosome 19 in RAB8A that were associated with MED16 protein expression and 5'-deoxy-5-fluorouridine response, the activated form of Capecitabine. RAB8A is a member of the RAS superfamily and implicated in tumorigenesis. MED16 is a coactivator involved in the transcriptional regulation of many RNA-polymerase II dependent genes and plays a role in Vitamin D reception, potentially affecting calcium homeostasis, cell proliferation, and cell differentiation. Thus, expression of MED16 may significantly alter transcription levels of RNA-polymerase II dependent genes and affect functions such as cell proliferation, which are abnormal in cancerous cell cycles. We predicted that RAB8A regulates the protein MED16 and impacts Capecitabine response. To test this hypothesis, we knocked down RAB8A with siRNA in MCF7 breast cancer cells and assessed its impacts on MED16 and MYC expression. Down regulation of RAB8A was verified with qPCR, and results revealed that RAB8A knockdown led to downstream effects of decreased MYC and MED16 expression at 46 and 72 hours, suggesting that RAB8A regulates MED16 with MYC signaling implications. Furthermore, decreased expression of MED16 is hypothesized to lead to poorer Capecitabine outcomes, implicating that MED16 is a contributor to Capecitabine response. Thus, results indicate that further research should be performed regarding the potential of MED16 to serve as a regulator affecting Capecitabine response and a potential prognostic biomarker for individuals treated with Capecitabine.

NOSBUSCH, SYDNYE (49)

Neurological analysis of mice with NMDA receptor mutations after infection with *Streptococcus pyogenes*

Advisor: Victoria A. Ploplis, Ph.D., W.M. Keck Center for Transgene Research,
Associate Director, Professor of Chemistry and Biochemistry, University of Notre Dame

Pediatric Autoimmune Neuropsychiatric Disorders (PANDAS) associated with Streptococcal infection is characterized by acute onset of intense anxiety, obsessive-compulsive issues, and/or motor tics post infection of a Group-A-Streptococcal (GAS) infection as a child. The objective of this study was to analyze behavioral changes in GAS infected wild type (WT) mice versus GAS infected NR2Bdelfb mice (NR2B subunit specifically deleted in the forebrain). Two strains of mice (n=20), WT and NR2Bdelfb, received either GAS culture supernatant or saline injections every three weeks. Behavior tests were conducted 1 week post injection and blood was collected 2 weeks post infection to determine anti-GAS antibody production. Western blot results of GAS supernatant incubated with sera from infected mice followed by goat anti-mouse IgG secondary antibody conjugated to HRP showed no reaction after the third injection boost of each challenge. Significant behavioral differences between the NR2Bdelfb and WT mice suggest more exploratory behavior in the NR2Bdelfb mice. This could be attributed to learning hindrance or decreased transmission of glutamate, which has implications in anxiolytics.

PAIETTA, ELISE (50)

Effect of Parasite Burden on the Survival of Yellow Baboons (*Papio cynocephalus*)

Advisor: Elizabeth Archie, Dept. of Biological Sciences, University of Notre Dame

Parasites are thought to exact a significant toll on animal health and survival. Parasite levels have been found to be enhanced by drought. Drought alone brings with it many imposing hardships to wildlife populations including loss of habitat, reduced food sources, and migration. This study aims to look at the effect that parasites have on individual survival during a drought. To accomplish this aim, we will use data on yellow baboons (*Papio cynocephalus*) from the Amboseli Baboon Research Project, a long-term population study, which experienced droughts in both 2015 and 2017. We hypothesize that increased parasite load, diversity, and richness will result in high mortality rates in the baboon population during the droughts. The parasites *Trichuris trichiura*, strongyles, *Abbreviata caucasica*, and *Streptopharagus pigmentatus* will be examined for this study. The additional hypothesis that the droughts caused reduced habitat and food quality will also be explored. Standard parasitological techniques will be used to measure parasite burdens in the baboons. We will combine this information with data on survival to test our hypotheses. Few studies have combined multiple factors, especially parasites, to investigate the effects of drought on a specific population. This study will help to bring insight to the transmission of infectious agents among a wild population during times of great environmental stress.

PETERSON, ERIK (ORAL PRESENTATION)

Analysis of a Century's Worth of AR Scorpii Photometry from DASCH and ASAS-SN

Advisor: Peter Garnavich, Dept. of Physics, University of Notre Dame

AR Scorpii (AR Sco) is a binary-star system containing the only known white dwarf pulsar. The system pulsates with a period of 1.97 minutes, brightening by a factor of 4, due to a rapidly-spinning magnetized white dwarf. The binary system has an orbital period of about 3.56 hours. We extend the observational baseline of AR Sco (which previously spanned back to 2005) back to the beginning of the twentieth century by compiling observations from the Digitized Harvard Astronomical Plate Collection (DASCH) running from the 1800s and the All-Sky Automated Survey for Supernovae (ASAS-SN) which is much more recent. By studying the orbital waveform across our baseline, we find that the average brightness of AR Sco remained constant over this time span indicating that the general waveform of AR Sco has remained consistent for more than a century. Additionally, Katz (2017) predicted a precessional period of the orbital light curve of 20 - 200 years that could be observed within a decade of observation. A previous study (Littlefield et al. 2017) attempted a verification of Katz's model for AR Sco but lacked the baseline to rigorously test it. We investigate Katz's hypothesis. We also constrain the rate of change of the orbital period.

PETRASKO, PHILLIP (51)

Exploring the Role of Multigenerational Obesity on Ovarian Cancer Metastasis

Phillip Petrasko (4), Tyvette Hilliard (1, 2), Marwa Asem (1, 2), Yueying Liu (1, 2), Jing Yang (1, 2), Jeff Johnson (1, 2), Gifty Marfowaa (4), Brooke Kowalski (1), Elinor Schnautz (1), Morgan McCabe (1) and M. Sharon Stack (1, 2)
(1) Department of Chemistry and Biochemistry, (2) Harper Cancer Research Institute, (3) Department of Biological Sciences, (4) Department of Pre-professional Studies, University of Notre Dame, Notre Dame, IN

Obesity is a worldwide epidemic with an increase in childhood obesity. Obesity has been implicated in many cancer types due to the abundance of nutrients and growth factors that aid tumor growth. Chronic inflammation found in obese patients has been linked to ovarian cancer (OvCa) incidence. OvCa is the most lethal gynecological cancer in U.S. women with poor survival rates due to intraperitoneal metastatic seeding of shed tumor cells from the primary tumor to secondary sites including the omentum. The goal of this study is to determine the maternal influence on the ovarian tumor microenvironment of subsequent generations. We utilized a pre-clinical murine model of diet-induced obesity that included maternal cohorts of C57BL/6 mice (dam) with intact host immunity fed either a control diet (10% Fat; Cohort A) or a high-fat diet (HFD; 40% Fat; Cohort B) and the resulting offspring fed either diet. Using this model, physical changes in the omentum, characterized using second harmonic generation microscopy, demonstrated a greater area of collagen mesh-work between openings in the omentum of mice exposed to a HFD, possibly allowing an increase in OvCa cell homing. Additionally, an allograft tumor study was performed using offspring fed either a control diet or a HFD to quantify site-specific metastatic success to the adipose-rich tissues of the peritoneal cavity including the omentum, gonadal fat, and the parietal peritoneum. Mice were injected with fluorescently tagged syngeneic ID8 murine ovarian cancer cells and disease progression was tracked for 8 weeks following injection. Abdominal organs were dissected, imaged *ex vivo*, and organ-specific tumor burden quantified by tumor area normalized to the weight of each organ. Common sites of ovarian cancer metastasis, including adipose-rich tissues and parietal peritoneum, were of interest. Overall, offspring fed a HFD displayed an increase in organ-specific tumor burden relative to offspring fed a control diet, regardless of dam diet. Furthermore, Cohort B offspring fed a HFD displayed higher omental tumor burden than Cohort A offspring fed a HFD. Together, the results provide support on how maternal obesity and subsequent exposure to a HFD can impact ovarian cancer metastasis.

PORTER, SAM (ORAL PRESENTATION)

Mass Measurements with Phase-Imaging Ion-Cyclotron-Resonance at Argonne National Laboratory

Advisor: Ani Aprahamian, Dept. of Physics, University of Notre Dame

Masses of atomic nuclei and mass differences of neutron rich or exotic atomic nuclei produced in fission are crucial to evaluating decay heats produced in nuclear reactors, as well as energy and light generation curves from events like the neutron star merger GW170817 in order to determine the existence of fission associated with such an event. Nuclear masses and observed solar r-process abundance distributions have been used to distinguish between potential sites for the r-process or the origin of the heavy elements. The primary contemporary tool for determining the mass of an ion with high precision is the Penning trap. A Penning trap is a device that exploits electric and magnetic fields to uniquely identify an ion's cyclotron frequency, from which the mass of the ion is determined. Typically, traps have provided the most precise measurements of masses, with error bars on the order of 10 keV. However, recently the Phase Imaging Ion Cyclotron Resonance (PI-ICR) method has been implemented to increase the precision of a measured mass. Using this technique, the frequency of a trapped ion is determined by the use of a position-sensitive micro-channel plate detector to record the position of the ions in the trap as a function of time. Using these time-dependent position measurements, we can determine the mass-dependent phase acquired by the trapped ions, and use this to determine the cyclotron frequency. Measurements of several neutron rich nuclear masses in the rare earth region produced from the spontaneous fission of 252Cf at Argonne National Laboratory's Canadian Penning Trap facility are presented.

PORTMANN, PATRICIA (52)

Increased survivorship of transgenic *Drosophila melanogaster* at high temperatures due to antifreeze proteins

Advisor: Henry Vu, Dept. of Biological Sciences, University of Notre Dame

Organismal adaptations that insects employ to increase their winter survivorship can also result in an increased ability to survive higher temperatures. Possible contributors to this increased heat tolerance could be their sub-zero adaptations such as high polyol concentrations, antifreeze proteins, and antifreeze glycolipids. To specifically investigate this phenomenon of increased heat tolerance due to winter adaptations at the organismal level, we tested transgenic *Drosophila melanogaster* that express antifreeze proteins from the fire-colored beetle, *Dendroides canadensis* (DAFPs). Transgenic *D. melanogaster* with individual DAFP-1 and DAFP-4 had increased survivorship compared to control flies after 24 hours when placed at 35–36.5°C. The 24-hour ULT_{50} (Upper Lethal Temperature at which 50% mortality occur) was calculated to be 36.3°C for DAFP-1 flies, 36.2°C for DAFP-4 flies, 35.4°C for wild-type controls, and 34.9°C for GAL4 controls. Additionally, we tested the survivorship of DAFP transgenic *D. melanogaster* reared at variable temperatures. *D. melanogaster* reared at 28°C had increased survivorship at 34.5–36.5°C compared to flies reared at 17°C and room temperature (20-22°C) after 24 hours. The 24-hour ULT_{50} was calculated to be 35.9°C, 35.0°C, and 35.1°C for DAFP-1 transgenic flies reared at 28°C, 20-22°C, and 17°C respectively. DAFP-4 transgenic flies demonstrated similar results with flies reared at 28°C, 20-22°C, and 17°C having ULT_{50} approximations of 35.7°C, 34.5°C, and 34.2°C, respectively. The results indicate that organismal adaptations employed by winter-adapted insects such as DAFP expression may have an alternative function contributing to the phenomenon of increased higher temperature survivorship in winter.

POTEREK, MARYA (53)

Modeling measles importation into the United States using international measles incidence and air passenger travel data

Advisor: Alex Perkins, Dept. of Biological Sciences, University of Notre Dame

Despite the elimination of endemic measles in the United States in the 1990s, the number of measles cases and outbreaks in the United States has begun to rise in recent years, as measles-mumps-rubella (MMR) vaccination rates in the US are declining and transmission internationally is on the rise. Measles is a highly infectious illness that can cause serious symptoms and even death in susceptible individuals, and cases imported to the US often result in large outbreaks that can be devastating to vulnerable populations. The majority of these imported cases reach the US via international passenger air travel through major metropolitan hubs. As a result, a significant proportion of US measles outbreak behavior can be modeled by connecting air travel data with location-specific measles transmission and prevalence statistics. This study sought to develop quantitative parameters for measles outbreak development in large US cities that are significant transit hubs, as influenced by case importation through plane travel. Assessing the probability of an individual's contact with and subsequent contraction of measles required data input from World Health Organization and Centers from Disease Control and Prevention (CDC) case and disease incidence reports in conjunction with open access global air network projections, which facilitated the establishment of country-specific importation probabilities using maximum likelihood estimation methods. Parameters were verified by comparison of model output, given a 90% data input, to existing CDC outbreak statistics, and revised accordingly. The resulting calibrated model has sufficient predictive abilities to assess the likelihood of a measles importation event and a resulting outbreak given situational and environmental data.

RICHARD, ALEX (ORAL PRESENTATION)

Detecting Levamisole-Adulterated Cocaine using a Paper Analytical Device

Alex Richard[1], Tracy-Lynn Lockwood[2], Marya Lieberman[2]
[1]Department of Preprofessional Studies, University of Notre Dame, IN
[2]Department of Chemistry and Biochemistry, University of Notre Dame, IN
COS-JAM 2019 Abstract

The veterinary anthelmintic medication levamisole has emerged as one of the prevalent cutting agents commonly found in cocaine. The presence of levamisole in cocaine samples has become increasingly widespread globally. In the United States, the DEA estimates that 80% of cocaine seized contains levamisole, prompting a 2009 public health alert from the Substance Abuse and Mental Health Services Administration. Similar statistics have been reported by regulatory agencies in the United Kingdom, Spain, and the Netherlands. Further, cases of severe adverse health effects including skin necrosis, neutropenia, and agranulocytosis have been reported as a result of levamisole-adulterated cocaine use. This rising prevalence of levamisole and its possible dangerous impacts emphasize the need for a low-cost and reliable method for detecting this cutting agent in cocaine samples. Current test kits for testing purity of cocaine can be expensive, unreliable, or unclear in their results, which possibly contributes to the use of cutting agents such as levamisole.

This research sought to adapt the Liebermann reagent test, which contains sodium nitrite and concentrated sulfuric acid and is known to be successful in detecting nitrogen rich compounds, on a Paper Analytical Device (PAD) to provide a means for identifying levamisole-adulterated cocaine. By adapting this test for use on the PAD, levamisole testing can be accomplished without analytical instrumentation and with limited resources. Results will examine the PAD's effectiveness in detecting levamisole and identifying the presence of levamisole as a cutting agent in cocaine.

RIVERA-LUNA, ANDREA (54)

Trans-splicing group I intron are an effective mediator of HIV-1 suppression

Advisor: Malcolm Fraser, Dept. of Biological Sciences, University of Notre Dame

In 2016, it was estimated that 36.7 million people were living with HIV, with an estimated 1.8 million new incidences that year.[1]. Of those living with HIV, 53% were receiving highly active antiretroviral therapy, or HAART.[2] The treatment, although effective in slowing the progression of the disease, does not eradicate the virus and leave open possibilities for escape mutations. The goal of this research is to fix this problem through transgenic modification. This is accomplished with a Group I intron, which uses two transesterification reactions to attach a code for apoptosis at a specific Uracil target. Four types of plasmid have been designed, each carrying the Group I intron with antisense guide sequences that target the Primer Activation Signal and Primer Binding Site (PAS/PBS) of HIV viral RNA. These introns have been coupled with a 3' exon encoding for ΔN-bax, a protein that induces apoptosis by inducing the release of cytochrome c from mitochondria, which activates initiation caspase 9 in the apoptotic caspase cascade.[3] By doing this, we expect not only suppress the activity of HIV, but effectively eradicate the virus from the host through a death-upon-infection strategy. We then have the medications and mechanisms to treat these immunosuppressed individuals as they recover.[4] Anti-HIV Group I splicing activity was assessed through RT-PCR. We were ultimately able to show expected band size results from the RT-PCR for 17/18 clones. The expected apoptotic pathway was assessed via Caspase 3 and BCA assays, and viral RNA suppression was quantified with TCID50 assays. These assays showed a correlation between elevated caspase activity and the suppression of HIV viral RNA in infected cells.

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ROFAEIL, MARTINA (ORAL PRESENTATION)

In-house generation of sequencing-grade trypsin for proteomics studies

Martina M. Rofaeil[1] and Matthew M. Champion[1]

[1]Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, IN.

Proteomics, the measurement of the proteins within biological systems, has become a crucial discipline of bioanalytical chemistry and biological understanding. A common approach is bottom-up proteomics, where protein mixtures are digested into peptides using proteases, then LC-MS/MS is performed to measure and fragment the peptides. Software is used to assemble the peptide MS/MS spectra into quantified proteins. Trypsin is the most common protease used due to its ability to cleave peptide chains after lysine and arginine amino acids. This reduces the assembly's complexity and generates peptides with advantageous properties in mass-spectrometry based proteomics. Sequencing grade trypsin is commercially available, but its high cost (>$1 /μg) makes some experiments impractical. A major attribute of commercial trypsin is increased resistance to autolysis, where trypsin cleaves itself after arginine and lysine residues, reducing activity. We sought to inexpensively and simply generate sequencing grade trypsin. We methylated bulk-grade trypsin by reductive iminidation with formaldehyde, which dimethylates primary amines, including lysine. Methylated trypsin is resistant to autolysis, temporally stable, and has reduced need for divalent cations for activity. Methylated trypsin remains catalytically active for several hours while trypsin autolyzes as seen by its rapid decline in catalytic activity within two hours. Methylated trypsin can be produced for approximately 1/1000th the cost of commercial trypsin, and we demonstrate that it exhibits virtually all of the efficacy and enzymatic activity of commercial trypsin. Analysis of this trypsin by MALDI-MS showed comparable modification to commercial trypsin, and we measured activity in steady-state kinetic assays and practical proteomics experiments. Digests of standard proteins with commercial and in-house trypsin showed insignificant differences in protein coverage and abundance, but a slight increase in under cleavage, which is indicative of slightly less activity than the commercial variant. A description of the designed method, data from practical experiments, and future modifications are described.

SANDERS, VY (55)

Investigating the Effect of Chronic HDACi via the TCF on the Stimulation of Stem Cell Proliferation in the Hippocampus

Md Suhail Alam, Boler-Parseghian Center for Rare and Neglected Diseases, Department of Biological Sciences, University of Notre Dame
Kasturi Haldar, Boler-Parseghian Center for Rare and Neglected Diseases, Department of Biological Sciences, University of Notre Dame

Kabuki Syndrome is an autosomal dominant disorder, caused by heterozygous loss of function mutations in either of two genes, KMT2D and KDM6A, which facilitate the opening of chromatin and gene expression. KMT2D is a histone methyltransferase that adds a methylation mark to H3K4, which leads to H3K4me3, an open chromatin mark. In a mouse model of Kabuki disease, which carries a mutation in Kmt2D gene, a deficiency of H3K4me3 activity leads to hippocampal memory defects and reduced neurogenesis. In this study, we utilized a mouse model of Kabuki disease and undertook molecular and immunohistochemical approaches to investigate the molecular mechanisms underlying hippocampal deficits. Quantitative PCR analysis was performed to study the expression profile of key neurogenesis as well as neuroinflammatory markers in the brain of Kabuki mice. As expected, Kabuki mice had ~50% reduction in Kmt2d transcript level. The transcript analysis revealed differences in the expression of key signature markers in the brain however, further investigation is required to better define the molecular changes associated with Kabuki disease. We also utilized DCX, a marker that is expressed in neuronal precursor cells and performed immunohistochemical analysis of the sub-granular zone of the hippocampus. Kabuki mice showed a reduced number of DCX positive neuronal precursor cells confirming reduced hippocampal neurogenesis as reported earlier. The length of the neurites originated from the DCX positive cell bodies were also reduced. Previously in the lab a triple combination formulation (TCF) of an HDACi was developed that allows the delivery of vorinostat across the blood brain barrier. The preliminary findings are not conclusive however; studies are in progress to investigate if pharmacological interventions could potentially help understanding the molecular mechanisms of impaired neurogenesis and hippocampal functions in Kabuki disease.

SERAPHIN, MICHAEL (ORAL PRESENTATION)

Generation of a Mouse Model for Group A Streptococcus Infections

Michael Seraphin
Major: Biochemistry, Theology (supplemental)
Advisor: Dr. Frank Castellino, Ph.D., W.M. Keck Center for Transgene Research,
Director, Professor of Chemistry and Biochemistry, University of Notre Dame

Group A streptococcus (GAS), a gram-positive bacterium, causes infections ranging from mild illnesses such as strep throat, to more severe illnesses such as necrotizing fasciitis and streptococcal toxic shock syndrome. GAS is highly human host-specific. Streptokinase (Sk), a protease secreted by GAS, in complex with plasminogen will cleave human plasminogen (hPg) but not mouse plasminogen (mPg). In this study, a mouse expressing a chimeric plasminogen (mPg hK2/hLC), was generated in order to create a mouse model for GAS infections. Plasma samples from the transgenic mice were analyzed by dot blot to determine levels of the chimeric plasminogen in circulation. A lysine-Sepharose affinity chromatography column was used to isolate the chimeric plasminogen from the mice. A western blot, using in-house antibody, was used to analyze protein from the column, which indicated the presence of the chimeric plasminogen, although at a lower concentration than expected. Activation assay techniques were used in order to determine if the chimeric protein was degrading while in circulation. The assays indicated that these transgenic mice, while expressing low amounts of the protein, can still be used to generate a functional model when supplemented with recombinant chimeric Pg.

SZYDLOWSKI, DANIEL (56)

Relationships between ecosystem primary productivity and sediment mineralization in temperate freshwater lakes

Authors: Daniel Szydlowski, Brittni Bertolet, Carly Olson, and Stuart Jones

Methane (CH_4) and carbon dioxide (CO_2) concentrations in the atmosphere have been positively linked to increasing global temperatures and climate change. Lakes are major contributors to these emissions (providing up to 20% of the global natural CH_4 emissions), and have large impacts on the carbon cycle. However, the contribution of lakes to atmospheric concentrations vary across lakes. Eutrophic lakes have been previously considered carbon sinks. This is because primary producers fix CO_2 into organic material, which is then buried in sediments via sedimentation. However, in sediments, anaerobic bacteria and Archaea can mineralize this organic material to CO_2 and CH_4, which has the potential to offset the amount of carbon buried. The objective of this research is to quantify the relationship between lake primary productivity, carbon sedimentation, and mineralization in anoxic sediments. We hypothesize that, in lakes, CH_4 and CO_2 production rates are positively correlated with lake primary productivity and sedimentation. To test this hypothesis, CH_4 and CO_2 accumulation rates were measured in 5 lakes at the University of Notre Dame Environmental Research Center throughout the summers of 2014 and 2015. Data was also collected on sedimentation rates and proxies of sedimentation, chlorophyll *a* concentrations and gross primary productivity rates. To quantify the relationship between primary productivity, sedimentation, and mineralization rates, we performed linear regressions between CH_4 and CO_2 accumulation rates and lake sedimentation and gross primary productivity. Our results indicate that these metrics are significantly related to CH_4 and CO_2 production, which could have wide-ranging implications for our understanding of both carbon cycling and climate change.

TALTAS, CAMILLE (ORAL PRESENTATION)

Markov Chains and Mixing Times on Colorings and Applications in Data Science

Advisor: David Galvin, Dept. of Mathematics, University of Notre Dame

The constant accumulation of data on our tastes, habits, and personal connections has substantially changed modern marketing strategies. Specifically, recommender systems have an integral role in personalizing advertising, by predicting user preferences and items of interest based on historical behavioral data. In my project, I analyzed an Amazon network that connects products which tend to be bought together. My premise was that if products tend to be bought together, advertising one of them entices the sale of the neighboring ones. Thus, in order to expand the reach of advertisements, I aimed to find a model that extends recommendations to products that are not frequently bought together.

In order to find an appropriate model for my network, I delved into the research I have been pursuing on Markov chains, mixing times, and graph theory for my undergraduate thesis. Over the past year, I have been studying Markov chains which sample colorings on graphs. I sought to improve the bound on the number of colors required for a chain to converge in logarithmic time to a stationary distribution. In particular, Glauber dynamics, which mixes rapidly to a uniform stationary distribution, models our recommendation system by sampling colorings that consider restrictions on the neighboring vertices. As a result, the stationary distribution uniformly assigns sets of customers to products which are not frequently bought together. Using Glauber dynamics is especially useful when handling big data as it only requires information about neighboring vertices.

Once put in practice, by diversifying user shopping habits, this recommender system will generate traffic and boost sales.

TOIVONEN, ANDREW (ORAL PRESENTATION)

Interpolation of odd beta-decay rates from even-even theoretical rates for nucleosynthesis applications

Advisor: Rebecca Surman, Dept. of Physics, University of Notre Dame

Beta decay rates, particularly those furthest from stability, are an essential part of nucleosynthesis calculations for extreme, super-massive stellar events. For such nuclei, however, experimental data is sparse and theoretical models are inconsistent with one another. In this theoretical and computational project, we started with the even-even beta decay rates of Mustonen and Engel and generated eight different sets of predicted odd-even, even-odd, and odd-odd beta decay rates. Some of the data sets we generated relied on theoretical data, some on experimental data, and others a combination of the two. When possible, the predictions were optimized to be the most accurate away from stability: in the region of sparse experimental data. We then investigated the impact of the different interpolations on abundance patterns from nucleosynthesis calculations run under four different initial conditions.

VALLERA, ALEXANDRA (57)

Functional validation of a candidate gene implicated in aridity tolerance in *Anopheles gambiae*

Advisor: Nora Besansky, Dept. of Biological Sciences, University of Notre Dame

Malaria is one of the foremost vector-borne diseases across the globe, having particularly devastating effects in the developing nations of Sub-Saharan Africa despite the use of insecticides to combat the spread of the disease. The study of inversions offers insight into the development of novel methods of malaria control targeted against its most important mosquito vector, *A. gambiae*. Reduced rates of recombination enable inversions to protect associations of genes that confer benefits under certain environmental conditions, such as aridity. The high correlation between the presence of the 2La inversion and aridity tolerance suggests that the 2La inversion is conferring aridity tolerance to *A. gambiae.* AGAP006026 is an ion channel gene located within the 2La rearrangement, and according to a prior association study in a natural population of A. gambiae, the allelic variant of this gene carried on the inverted orientation of 2La is highly correlated with aridity tolerance. In order to confirm a causal relationship between this allelic variant and aridity tolerance, RNAi procedures were used to knockdown the target gene in a laboratory population homozygous for 2La. RNAi was triggered by the exogenous introduction of dsRNA into *A. gambiae,* which is digested *in vivo* into siRNA molecules which limit the expression of the target gene. Ongoing experiments are working to confirm knockdown by qPCR, and physiological assays of dsRNA-treated and mock-injected mosquitoes will be performed to test for time-to-death under desiccating conditions. We hypothesize that the mosquitoes with knocked-down AGAP006026 will have a lower survival time in the presence of the desiccant agent, thus displaying decreased aridity tolerance due to the inactivation of target gene AGAP006026.

VERHEY, ERIK (58)

Virtual, augmented, and mixed reality applications in orthopaedic surgery

Jens T. Verhey[1] , Jack M. Haglin[1], Erik M. Verhey[2], David E. Hartigan, MD[1,3]

Mayo Clinic Alix School of Medicine, Scottsdale, AZ[1]
University of Notre Dame, Notre Dame, IN[2]
Department of Orthopedic Surgery, Mayo Clinic, Phoenix, AZ[3]

Corresponding Author:

David E. Hartigan, MD

Innovation in computer-assisted surgery (CAS) and surgical training aims to increase operative accuracy and improve patient safety by decreasing procedure-related complications. CAS has been demonstrated to improve surgical outcomes by providing more accurate measurements and enhanced spatial position feedback of surgical tools relative to anatomical features and targets. The application of reality technologies, including virtual reality (VR), augmented reality (AR), and mixed reality (MR) to computer-based surgical systems, has begun to revolutionize orthopaedic training and practice. Trainees now have authentic and highly interactive operative simulations without the need for supervision. The practicing surgeon is better able to (i) pre-operatively plan and intra-operatively navigate without the use of fluoroscopy, (ii) gain access to three-dimensional reconstructions of patient imaging within view of the surgical field, and (iii) remotely interact with colleagues located outside the operating room. Virtual reality techniques have been previously reviewed for the training of surgical residents. However, there have not been any reviews exploring the applications for virtual, augmented, and mixed reality in orthopaedic practice and training. This review provides a current and comprehensive examination of the reality technologies and their applications in orthopaedic surgery.

VINCENT, NOEL (59)

Fighting for Better Drug Detection: Detecting Anthraquinone and Anthraquinone-like Groups Using Vanadyl (IV) Sulfate

Advisor: Nils Oberhof, Dept. of Chemistry and Biochemistry, University of Notre Dame

Counterfeit and substandard medication, and the illicit supply chains they flow through, continue to complicate global health issues. The Paper Analytical Device (PAD), developed at the University of Notre Dame has allowed for onsite detection of these harmful drugs by citizens at a fraction of the cost of high-performance liquid chromatography. The PAD works by maintaining twelve lanes of reactants, each over which will react to generate a positive or negative color test depending on the functional groups being present. The PAD is run by applying the medication across a marked swipeline, effectively reaching each of the twelve lanes, before placing the PAD vertically in a source of water. Capillary action then results in the water moving up the lanes while mixing the reactants with the unknown drug sample. The colored barcode generated can be used to identify medication. Innovations in these lanes allow for better drug detection and detection of signature functional groups. In this experiment, Zirconyl (IV) Nitrate or Vanadyl (IV) Sulfate are introduced to the PAD to react with medications with anthraquinone(like) groups. Five antibiotics, Rifampicin, Doxycycline, Tetracycline, Levofloxacin, and Oxytetracycline, each having anthraquinone or similar groups, were selected to react with Zirconyl (IV) Nitrate and Vanadyl (IV) Sulfate. Unique, and potentially characteristic, color codes were produced.

WALTERS, MAGDALENE (60)

Public health impact of vaccination with Dengvaxia in the presence of intra-urban variation in dengue virus transmission

Authors: Magdalene K. Walters, T. Alex Perkins

Dengvaxia from Sanofi Pasteur is currently the only licensed dengue vaccine. Results from phase-III trials indicate that people with no history of natural dengue virus (DENV) infection who receive Dengvaxia experience an elevated risk for severe disease upon subsequent natural infection. This finding has shed light on the importance of spatial variation in DENV transmission history, with this vaccine only recommended for use in areas with a high probability of prior DENV infection among potential vaccinnees. This recommendation has prompted efforts to measure DENV transmission intensity through the analysis of serological survey data. However, DENV transmission is known to be highly spatially heterogeneous, even at intra-urban scales. We performed a modeling analysis to understand whether spatial aggregation of serological data at the scale of a city could lead to unintended harm in the presence of spatial heterogeneity in DENV transmission below the scale of the city as a whole. We used a modified SIR model that allows for up to four distinct DENV infections over a person's lifetime to examine the differential impacts of vaccination on two sub-city communities with different transmission intensities but connected by human mobility. The effectiveness of vaccination campaigns was evaluated using the proportion of cases averted. Results indicate that each community benefits greatly when the high-transmission community is fully vaccinated. These benefits are maintained until the low-transmission community achieves approximately 70% vaccination coverage, after which there are diminishing returns in terms of proportion of cases averted. This work has implications for vaccination campaigns in cities in which there is spatial heterogeneity in transmission that is unaccounted for in the aggregation of serological data at a city-wide scale.

WEINRICH, JACQUELINE (61)

Investigating the role of two novel prostate cancer drivers in a mouse model

Advisor: Xin Lu, Dept. of Biological Sciences, University of Notre Dame

Prostate cancer is the second most lethal cancer for men, with over 160,000 new cases in the United States alone every year. Current therapeutic approaches include chemotherapy, radiation, and surgical castration in some cases, but primarily focus on androgen deprivation therapy due to the key role of the hormone androgen in the progression of prostate cancer. However, if cancers are resistant to androgen deprivation therapy, further treatments have not been shown to be effective. 90% of these cancers ultimately metastasize to bone and cause significant mortality. Thus the importance of providing new treatments directed to specific targets in prostate cancer progression cannot be overstated. SPOP is the most commonly found mutated protein in human prostate cancer (PCa) samples. SPOP mutation is mutually exclusive with other common genetic aberrations in human PCa, therefore SPOP mutation demarcates an individual subtype of PCa. Within the SPOP mutant PCa subtype, the most common coincident genetic aberration is CHD1 homozygous loss. Though the clinical data points to SPOP/CHD1 interaction, and individual studies of each protein have been conducted, there is no published histopathological study of the interaction of SPOP and CHD1. Therefore, the Lu lab attempted to create a transgenic mouse model with SPOP and CHD1 knocked out by a tissue-specific Cre promoter, to study the specific effects of these proteins in the prostate. Here, we attempted to confirm SPOP and CHD1 knockout using multiple techniques, including multiple trials of immunohistochemistry (IHC), Western Blot, qPCR and RT-PCR for mRNA analysis, and Flow Cytometry, ultimately finding success using the IHC and RT-PCR method. Additionally, we assessed downstream targets and proliferation of different models. This data provides insight into the mechanism of this commonly implicated genotype in PCa, with the hope of improving outcomes for men with castrate-resistant prostate cancer.

WEYHMILLER, SIERRA (62)

How "Squishy" are Nuclei? Finding an Accurate K_τ

Advisor: Umesh Garg, Dept. of Physics, University of Notre Dame

Astrophysical models of neutron stars require the nuclear equation of state for physical input, whose accuracy is dependent the value of the nuclear incompressibility of infinite matter, K_∞. An important component of this value is the asymmetry term, K_τ, which is critical to understanding systems with a large imbalance of protons and neutrons. Measurements on the isoscalar giant monopole resonance in finite nuclei allow for the extraction of these values. Recently, a group at Texas A&M claimed that heavier calcium isotopes are more incompressible than lighter isotopes, indicating a positive K_τ. This is in direct opposition to decades of research and theory on nuclear matter. The purpose of this study is to either support or refute this claim. To do so, we have conducted a simultaneous study of the giant monopole resonance (GMR), a form of radial oscillations in the nuclei, of the ^{40,42,44,48}Ca nuclei. The isotopes were excited into this state by bombarding the isotope with 386 MeV α -particles. Using the spectrometer, Grand Raiden, the α -particles were momentum-analyzed after scattering on the targets. Using relativistic kinematics, the excitation energies of the recoiling calcium nuclei were reconstructed. Angular distributions were extracted, and contributions from hydroxide contamination were found in the ^{48}Ca foil. It is essential that the contaminant's contribution to the spectra is subtracted because the multipole decomposition analysis necessary to translate angular distributions to GMR strength distributions would be altered by the contaminants. To do this, the amount of oxygen nuclei present in the foil must be determined, which can be found from the published cross sections for ^{16}O(α, α) elastic scattering, various experimental parameters, and the number of events which are solely from ^{16}O(α, α) elastic scattering. In this work, I have developed an efficient way of accounting for oxygen contamination in the target foils.

WHALEN, JACQUELINE (63)

The relationship between angler socio-economic and lake ecological characteristics in northern Wisconsin

Advisor: Colin Dassow, Dept. of Biological Sciences, University of Notre Dame

Recreational fisheries act as complex social-ecological systems where biophysical and social components interact over a large spatial scale. Anglers function as social agents in the system whose actions and choices have large impacts on resource availability and management policies. A key link between the ecological and social components of the social-ecological system is where they choose to fish. The objective of this study was to characterize and understand the respective relationships between the socio-economic and ecological characteristics of anglers and lakes. Angler diversity as a response variable was measured as the number of unique regions that anglers had traveled from. Data was collected from over a hundred surveys of angler visits to sixteen different lakes located in northern Wisconsin spanning differing degrees of urban development, accessibility, and fish diversity. Ecological data such as fish species presence and lake size were collected for each lake in the analysis. Recent census data including mean annual income, percent population in poverty, and percent population unemployed were accessed for the home zip codes of the surveyed anglers. Linear regression and ANOVA analyses were used to describe relationships between angler site choice and the ecological and socio-economic characteristics of the site. Angler socio-economic characteristics did not predict site choice. Certain ecological characteristics such as the presence of key species, fish diversity, and lake size did predict angler diversity. In general, the lake characteristics examined did not predict angler site choice. The lakes received differing amounts of angler fishing effort, but our analyses cannot fully explain what drives these differences. Some limitations that may have affected the results include the small sample size, the large number of correlated variables that may have confounding effects, and the limited resolution of knowledge about actual angler socio-economic statuses and experiences.

WHITE, ABIGAIL (64)

The impact of row-crop agriculture on the biodiversity of stream macroinvertebrates

Abigail A. White, Matt T. Trentman, Jennifer L. Tank

The richness and diversity of stream macroinvertebrates can be used as a metric of ecosystem health because the ability to survive in impacted streams varies among species. Land use, such as row-crop agriculture, can negatively impact streams by increasing sediment loads from erosion, reducing canopy cover in riparian zones, and altering substrate heterogeneity via the addition of finer sediments. As such, benthic substrate can limit the diversity of macroinvertebrate communities, especially in agricultural streams. We investigated the impacts of land use on stream macroinvertebrates at nine sites in the Paw Paw River Watershed (MI) using Hester-Dendy (H-D) multiplate samplers, which gave us an opportunity to look beyond substrate availability as a driver of abundance, as H-D samplers provide artificial substrate for macroinvertebrate colonization. We placed replicate samplers across the stream network with a range of upstream land use, either as agriculture (44-88%), or forest (8-47%), as well as riparian canopy cover (0-98%). We predicted that sites with more agriculture would have lower richness and diversity, and that higher canopy cover would increase diversity due to the addition of allochthonous organic matter to the stream, which favors detritivores. The H-D samplers were incubated for six weeks in Fall 2018, and macroinvertebrates were counted and identified to the lowest possible taxonomic unit. Shannon's diversity index was negatively correlated with the percentage of row-crop agriculture ($p<0.001$), and increased marginally with canopy cover ($p=0.08$). Despite the constant substrate provided by the H-D samplers, we found that row-crop agriculture still negatively impacts aquatic macroinvertebrate diversity. We predict that other factors such as increased sediment loads from erosion (i.e., reduced water clarity) and poor water quality (e.g., pesticide and fertilizer contamination) are also important drivers of macroinvertebrate community structure in Midwestern streams.

WILKINSON, PAUL (65)

The role of aging collagen in the metastasis of ovarian cancer

Paul Wilkinson [1], Preston Carey [1], Elizabeth Harper [1,2], Elizabeth Loughran [1,2], M. Sharon Stack[1]
[1] Department of Chemistry and Biochemistry, [2] Integrated Biomedical Sciences Program

Ovarian cancer (OvCa), the deadliest gynecological cancer, spreads throughout the peritoneal cavity and causes extensive metastatic sites before it can be diagnosed in most patients. Greater research on the impact of aging on the OvCa tumor microenvironment could lead to new methods of detection of OvCa in elderly patients and more efficient treatment of these patients before widespread metastasis. One model used to analyze the impact of aging on OvCa metastasis is using observing the degradation of collagen over time. Collagen is abundant in areas of OvCa metastasis such as the omentum and peritoneum. Using cohorts of young mice (three to six months old) and old mice (twenty to twenty-three months old), collagen samples can be extracted and then used in models to show OvCa's impact on aged versus young collagen. This study analyzes the impact of collagen degradation on both cancer cell transport as well as further degradation of collagen by matrix metalloproteinases (MMPs) that are secreted by OvCa cells. **Focus one** of this study will use a biotin-tagged peptide to visualize how tumor cells remodel the microenvironment. Tissues from the omentum and peritoneum containing collagen concentrations will be sectioned, stained with a collagen hybridizing peptide (CHP). The new tech biotin-tagged peptide hybridizes denatured collagen, which allows for a clear visual of how the microenvironment is changing. Tissues will also be stained with more conventional antibodies later, such as □-LOX, and then examined using second harmonic generation imaging. This will allow for imaging of the peptide with a fluorescent tag and *ex vivo* experiments involving the extraction of collagen from the peritoneal cavity; providing an accurate relationship between OvCa cells and aged collagen in the microenvironment. **Focus two** of this study will examine the impact of MMPs on collagen extracted from both young and aged mice. Collagen samples from both young and aged mice cohorts will be incubated with the same concentration MMP-1 enzyme which will cleave the collagen proteins at specific sites. The rate of this cleavage can be calculated using hydroxyproline assays as the content of hydroxyproline present after cleavage can be used to determine the rate of cleavage using Michaelis-Menten kinetic analysis. This analysis will allow the efficiency of MMP-1 cleavage to be determined which can give an indication of the efficiency of other MMPs that are secreted by OvCa. In order to further relate this data to peritoneal and omental OvCa models, an *ex vivo* analysis will be conducted using tissues sectioned from the peritoneum and omentum. These tissues will be sectioned, incubated with equal concentrations of MMP-1, and then again analyzed using a hydroxyproline assay. The assay will help determine the kinetics of degradation on peritoneal tissue by the MMP. These tissues will then be imaged under a scanning electron microscope to provide a qualitative analysis of degradation of MMPs to accompany the quantitative analysis provided by the hydroxyproline assay and Michaelis-Menten analysis.

YAN, LIHAO (66)

Development and Simulation of the ND Cube Active-Target Time Projection Chamber

Advisor: Tan Ahn, Dept. of Physics, University of Notre Dame

Studies of detectors are important for major advances in nuclear physics. To make such advances, detectors with high efficiency are needed to study reactions with radioactive beams that have low intensities. At the University of Notre Dame, we are developing an Active Target Time Projection Chamber (TPC) called the ND Cube which improves the efficiency by using a thick gas target with track imaging. The ND Cube can track reaction trajectories and provide good resolution for those reactions. For the development of the ND Cube, I designed a printed circuit board (PCB) named ZAP that receives the electronic signals from the Micromegas and connects those signals to a data acquisition card called the AsAd. The AsAd digitizes the signal which is then stored on a computer for future analysis. To hold the AsAd boards in place, I also designed a supporting box attached to the detector. For the simulation part of my project, I calculated the electric field and the behavior of the electron drift lines inside the ND Cube using the finite element analysis software COMSOL and CERN's Garfield++ toolkit. We determined the resolution and the expected transport of the electrons in the detector. We found a standard deviation of $\sigma = \pm 0.85$ cm for each electron drifting in 55 cm of air at 1 atm, which determines the resolution of our imaged tracks. For future experiments, the simulation result will be compared with the electron signals collected to calculate the efficiency and the resolution of the ND Cube.

ZHANG, GRACE (67)

Investigating the regulation of atoh7 expression in the regenerating adult zebrafish retina

Advisor: David Hyde, University of Notre Dame Dept. of Biological Sciences

In humans, neurogenesis is limited to retinal development, while many lower vertebrate species, like *Danio rerio* (zebrafish) rapidly regenerate damaged retinal neurons to restore vision. If mechanisms of retinal regeneration in zebrafish are understood, therapies may be developed to overcome blindness in the structurally analogous human retina. In adult zebrafish, death of retinal neurons induces Müller glia, a stem-like retinal cell, to proliferate to produce neuronal progenitor cells (NPCs), which then differentiate into retinal neurons. Atoh7, a factor regulating ganglion cell commitment during retinal development is also upregulated in the regenerating retina. While the regulation and function of Atoh7 in the regenerating retina has not been studied, it is known that Notch signaling represses *atoh7* expression during development. Thus, to test whether Notch signaling regulates *atoh7* expression and thereby cell fate determination, Tg[*atoh7*:GFP]; Tg[*her4*:RFP] double transgenic fish light-damaged for 48 hours were intraperitoneally injected with the gamma-secretase inhibitor, RO4929097, or its vehicle control, DMSO. Retinal sections revealed that *atoh7*:GFP and the Notch-downstream target, *her4*:RFP, were expressed in distinct NPCs at 72 hours of light-treatment. Initial observation suggests that more *atoh7*:GFP-positive cells are present in R04929097 retinas relative to DMSO-treated fish. Additionally, preliminary quantitative real-time PCR data revealed increased expression levels of *atoh7* and ganglion cell marker *alcama* in RO4929097-injected retinas relative to DMSO controls. Similarly, commitment factors for amacrine cells, *ptf1a* and *foxn4*, and proliferation marker, *pcna*, were also upregulated. In contrast, *nrl*, a rod photoreceptor commitment factor, decreased in expression in RO4929097-injected retinas relative to DMSO controls. To summarize, our preliminary data suggest that Notch inhibition increases proliferation as well as commitment to ganglion and amacrine cells at the expense of *nrl*-positive photoreceptors.

Keywords: Zebrafish; Retinal Regeneration; Development; Cell Fate; *atoh7*

ZHUANG, YI (68)

The Black-Scholes-Merton Model: Theory and Application in Chinese Option Market

Advisor: Alex Himonas, Dept. of Mathematics, University of Notre Dame

The Black-Scholes-Merton (BSM) model, developed by Fisher Black, a world-renowned economist from University of Chicago, Myron Scholes and Robert Merton, two famous economist from Massachusetts Institute of Technology, who won the 1997 Nobel Prize in Economics, is one of the most important concepts in modern financial theory. It works for pricing option or other stock derivatives. It is still now widely used and many of the scholars nowadays work on its implications and applications in mathematical finance.

The first part of this research investigates the theory of the classical Black- Scholes-Merton model, from the vanilla one-period binomial model to the multiperiod discrete-time model. Using the method of replicating portfolio, it revisits the derivation of the Black-Scholes-Merton model. Then it studies the construction of Brownian motion – wiener process as the limit of random walks. This research then derives the Black-Scholes-Merton Partial Differential Equation using the method of replicating portfolio and gives a solution to the PDE.

In the second part, this research studies the aspiring Chinese option Market – its characteristics and differences from US option market. This research contends that the assumption of constant volatility in the classical BSM model fails in the Chinese option market and gives two stochastic (non-constant) volatility models – the Heston model and the GARCH model as modifications of the classical BSM model. This research also offers technical specifications for realizing these two models and empirical analysis for pricing accuracies in real Chinese option markets. In summary, this research concludes that the stochastic volatility model is a superior model for pricing Chinese options.

SHEEHAN, COLIN (69)

Aberrant endocytosis leads to the loss of normal mitotic spindle orientation during epithelial glandular morphogenesis

Biological Sciences Major, College of Science
Research Advisor: Dr. Crislyn D'Souza-Schorey, Ph.D.
Co-Authors: Dr. James Clancy, Ph.D., Christopher Tricarico

Epithelial cells form tissues with many functions, including secretion and environmental separation and protection. Glandular epithelial tissues comprise of cysts and tubules that are formed from a polarized, single-epithelial cell layer surrounding a central, fluid-filled lumen. The pathways regulating key processes in epithelial tissue morphogenesis such as mitotic spindle formation are incompletely understood, but are important to investigate, as their dysregulation is a signature of epithelial tumors. Here, we describe a signaling axis that manifests in a defect in mitotic spindle orientation during epithelial growth and cystogenesis. We found that activation of the small GTPase ADP ribosylation factor 6 (ARF6) results in the sustained internalization of cell-surface components such as the cMet receptor and the cell-adhesion molecule E-cadherin. The spindle orientation defect arising from elevated levels of ARF6–GTP required an increase in cMet endocytosis, but was independent of E-cadherin internalization or elevated extracellular signal-regulated kinase (ERK) activity resulting from internalized receptor signaling on endosomes. Misorientation of the mitotic spindle resulted in the development of epithelial cysts with structural abnormalities, the most conspicuous of which was the presence of multiple intercellular lumens. Abnormal mitotic spindle orientation was necessary but insufficient to disrupt glandular development, as blocking the strong pro-survival signal resulting from ERK hyperactivation yielded structurally normal cysts despite continued manifestation of spindle orientation defects. Our findings highlight a previously unknown link between ARF6 activation, cMet receptor internalization, and mitotic spindle orientation during epithelial glandular morphogenesis.

Spirit of Science Presenters—1:00-1:45 pm

Effects of Acid Rain
Akash Agarwal, Concord Intermediate School

Inhibitors of Metastasis Pathways
Matias Dahl, Schmucker Middle School

Distracted Driving
Wyatt Keller, New Prairie Middle School

The Power of Noise: Do Sound Waves Affect the Viscosity of Non-Newtonian Fluids
Greta Lannon, Schmucker Middle School

Chemistry of Soap
Dessie Mikels-Carrasco, NW Regional Home Schools

How does the material of a microphone screen affect sound?
Evelyn Shrout, Discovery Middle School

Is Whitening Toothpaste Worth It?
Lillie Veldman, Holy Family School