UNIVERSITY OF NOTRE DAME

# Colleges of Science & Engineering Joint Annual Meeting

## Inaugural COSE-JAM for Graduate Students & Postdoctoral Fellows

**Friday – December 8, 2017**

**Jordan Hall**

## **SCHEDULE:**

*Morning Session (10-12:00pm):* 45 poster presentations in Jordan Galleria
(continental breakfast/snacks/drinks in Galleria; posters taken down by 2pm)

Informal Q&A Informational Tables – IDEA Center, Office for Postdoctoral Scholars, Graduate Career Services, Office of Grants and Fellowships

*Lunch (12-1:30pm):* Jordan Galleria – participants, discussants, moderators, co-authors, etc.

*Seminar & Panel Discussion (12:15-1:15pm):* 101 Jordan – career development & advice, etc.

"Post-Graduate Education as a Road to Entrepreneurship"
(Bryan Ritchie, James Thompson & Richard Cox, IDEA Center)

*Afternoon Session (1:30-3:50pm):* 14 podium presentations in Jordan auditoriums (101 & 105)
(snacks/drinks in Galleria; two mixed-subject concurrent oral sessions)

*Post-Meeting Social (3:45-5:00pm):* Jordan Galleria – opportunities for informal interactions
(snacks/soft drinks/beer/wine)

Funding for this joint event was provided by the Colleges of Science and Engineering. Many thanks to the following for help and support: Dean Mary Galvin, Dean Peter Kilpatrick, Associate Dean Mike Hildreth, Associate Dean Mark McCready, Associate Provost & VP Bryan Ritchie, Associate VP James Thompson, Richard Cox, Crislyn D'Souza-Schorey, Brian Baker, Andrew Sommese, Peter Garnavich, Jeffrey Diller, Ken Christiansen, Patrick Flynn, Joannes Westerlink, Ed Maginn, Thomas Fuja, Rebecca Wingert, Holly Goodson, Glen Niebur, Sharon Stack, Brandon Ashfeld, Mark Caprio, Fang Liu, Peter Cholak, Tim Ovaert, Gregory Madey, Antonio Simonetti, William Schneider, Vijay Gupta, Dom Chaloner, Allen Utterback, Lisa Mercurio, Kim Kirkpatrick, Valli Sarveswaran, Larry Westfall, Karen Slaggert, Charles Powell, Samantha Lee, Hannah Babbini, Susan Coiner-Collier, Tyvette Hilliard, Melissa Hoffbauer, the CGSO, Emily Nett, Tammi Freehling, Deanna McCool, and the myriad graduate student and postdoctoral researchers who contributed to the success of this first-ever joint college event.

# PANEL DISCUSSANTS (lunchtime at 12:15-1:15pm – 101 Jordan)

**Bryan K. Ritchie**, M.B.A., Ph.D., Vice President and Associate Provost for Innovation. Dr. Ritchie was appointed Notre Dame's first VP and associate provost for innovation in 2017. Leading the University's IDEA (Innovation, Discovery, and Enterprise Acceleration) Center, he works closely with deans, alumni, faculty, and students to promote a culture of innovation, entrepreneurship, and commercialization.

Dr. Ritchie's major responsibilities as head of the IDEA Center include directing the University's technology transfer enterprise as well as ND's Innovation Park, a commercial accelerator designed to help Notre Dame researchers and others bring their discoveries to market. Beyond the IDEA Center, he provides oversight for Notre Dame California, through which the University is expanding its presence across the state from its facility in Silicon Valley.

With extensive experience in both industry and the academy, Ritchie came to ND from the venture capital firm GrowthSPORT. As president and CEO, he guided its investing activities, focusing primarily on seed-stage technology companies. Ritchie has formed two information technology companies of his own during his career and also held management positions with Century Software, Dayna Communications, IBM, Novell, IOMEGA, Megahertz, and 3Com. He has consulted for Eli Lilly, Astra Zeneca, Ericcson, Seagate, Verizon, Givaudan, and over 100 other companies.

Prior to co-founding GrowthSPORT, Ritchie spent four years directing technology commercialization at the University of Utah, first as associate vice president for technology venture development and then as associate vice president for research. He oversaw more than 60 new startups, more than $700 million in investment and grants, an average of 90 licenses per year, and 90+ patents per year.

Ritchie is a graduate of the University of Nevada, Las Vegas, and holds an M.B.A. from Brigham Young University's Marriott School of Management and a Ph.D. in political economy from Emory University. As a member of the faculty at Michigan State University, he rose from assistant to associate to full professor of political economy, served as chair of International Relations and was part of the core faculty of the Asian Studies Center. In addition, he served as director or co-director of two student entrepreneurship programs and as associate director for external strategy of the MSU BioEconomy Network, which coordinates the university's initiatives to promote Michigan's bioeconomy through research, policy and economic analysis, education, corporate and government collaborations, and commercialization.

**James E. Thompson**, M.S., is Associate Vice President for Innovation and Executive Director, Commercialization Engine Team. James has over 17 years' experience in management, business development, marketing, biotechnology research and quality systems. Most recently James was the Interim Executive Director of the Technology & Venture Commercialization office (TVC) at the University of Utah. While at the TVC, in multiple roles including the Interim Executive Director, Director Engineering Team and Business and Technology Manager, James helped to develop and implement a stage gated, milestone driven commercialization process called the Utah Model of Commercialization or affectionately called the Commercialization Engine. The Commercialization Engine is a system to assisted companies with licenses to university owned technologies successfully commercialize the licensed tech (providing assistance in the areas of strategic planning, funding, problem solution fit, product market fit, recruitment of leadership and more). The system substantially improved both internal and external customer service while increasing the commercialization activity of technologies developed and owned by the University of Utah.

Prior to the University of Utah, James was the Director of Business Development and Director of New Product Development for chemical company (Frontier Scientific) and a research reagents company (Echelon Biosciences). In these companies James released over 200 new products (resulting in an increase of total product offering by 15% and set up collaborations with over 27 entities.

Thompson has also founded four companies, three of which are still in business. Quansys Biosciences, still in business, develops and sells test kits used in the pharmaceutical, clinical and academic research use markets. PetroBio Tech, no longer in business, distributed a fuel additive and performed services in the oil and gas industry cleaning crude oil storage tanks using a proprietary solvent/surfactant blend. Energy Innovation Services, Inc., currently the President, was founded to commercialize a patented surfactant/solvent blend + water conditioner in the oil/gas industry. The Company is focused on manufacturing products and working with distributors to provide the service to oil/gas operators. Finally, Allerief, Inc., currently the President, is focused on developing an over the counter remedy to reduce severity of food-specific allergic reactions.

James has an M.S. and B.S. in Biology from Utah State University and an A.S. in Biology from BYU-Idaho.

**Richard Cox**, M.B.A., is the Director of the Office of Technology Commercialization at the IDEA Center. With 27 years commercializing research technologies, Dick Cox has led and served four major universities in moving technology from the lab bench to the marketplace. Joining Notre Dame in 2008 as the Director of the Office of Technology Transfer, Dick has overseen the doubling of licenses and licensing revenues and initiated the University's movement into equity licensing, leading to a current portfolio of 20 equity holdings. During a period of rapid growth in entrepreneurship and related programs across campus, Dick helped position OTT as a valued resource, contributor, and partner.

Prior to his work with Notre Dame, Dick served as Director of Technology Transfer and Economic Development at the University of Hawaii, Director of the Intellectual Property Management Office at the University of South Carolina, and Director of Marketing at the University of Tennessee Research Corporation.

Earlier in his career, Dick was the Director of Marketing for the National Technology Transfer Center, the premier market research organization for NASA and other federal agencies. Dick's experience extends to industry as well, where he worked for Milliken & Company as a manufacturing supervisor in the US's leading privately owned textile manufacturing company, at Lockheed Martin in its Marietta, Georgia aircraft manufacturing and maintenance facility as an Industrial Engineer, and as an entrepreneur and founder for Spectrum Mortgage Corporation, specializing in residential mortgage financing. In addition, Dick worked for two years with the former Anthony B. Cassedy & Associates consulting firm, contributing to system improvements in companies in the consumer electronics and defense electronics spaces.

Dick is a member of the Advisory Board of TechConnect, a global technology outreach development organization moving technology to industry from NASA, the National Science Foundation, National Institutes of Health, Department of Defense, Department of Energy and many others. He is a long time member of the Association of University Technology Managers, serving on various committees and as a speaker at both regional and national meetings. Dick's passion for academic technology commercialization also carries over into the classroom, where he has been a frequent guest lecturer on technology licensing as a business model – and also as an exciting and rewarding career option.

Cox earned a bachelor's degree in industrial management and a M.B.A. degree with dual concentrations in finance and new venture analysis from the University of Tennessee.

# MORNING POSTER SESSION (10am-12:00pm – Jordan Galleria)

**Wendy Alvarez Barrios**: Integrative Platform for the Investigation and Modeling of the Subcellular Changes of Single Cells during Metastatic Mechanical Arrest in the Brain Vasculature

**Emily Ann Amenson-Lamar**: Differential Proteomics Study of Fetal Bovine Serum using CZE-MS/MS

**David Burney**: What Moderately Volatile Elements in Lunar Basalts Reveal about the Moon's History

**Katelyn Carothers**: Exploring the Role of the Multi-Functional Cysteine Protease SpeB in Cardiac Tissue during Group A Streptococcal Infection

**Warren Chatwin**: Episodic Hybrid Advantage Keeps Species Boundaries Low in Oaks

**Alexandra Chirakos**: Negative Regulation of ESX-1 Secretion by EspF is Mediated by N-Terminal Acetylation

**Loretta Corcoran**: Chemical Characterization of Altered and Unaltered Uraninites from various Geological Settings

**Karl Cronberger**: KREEPy Moon Rocks: KREEP Basalt Petrogenesis

**Kimberly Curtis**: Effects of NS1643 on Senescence in Human Breast Cancer Metastases to Trabecular Bone

**Micah Ferrell**: Identification of an N-Acetyl Transferase from *Mycobacterium marinum* with Activity towards the Virulence Factor EsxA (ESAT-6)

**Ian Guldner**: Fractalkine Receptor Downregulation in Heterogeneous Brain Metastasis-Associated Myeloid Cells Induces Tumor-Promoting Interferon Response

**Timothy Gunther**: Calcium and Iron Isotope Analysis of Uraninite and Other Uranium-Rich Materials: Development of Potential New Forensic Isotope Tracer Methods

**Elizabeth Harper**: Aging Promotes Changes to Peritoneal and Omental Collagen Structure that Contribute to Increased Ovarian Cancer Metastatic Success

**Tyvette Hilliard**: Mesothelin Expression Impacts the Metastatic Success of Ovarian Cancer

**Simon Hinnekens**: Kinematic Analysis of Lunge Characteristics in Young, Healthy Subjects

**Melissa Hoffbauer**: A Series of Iron Carbenes and their Unique Reactivity with Styrene

**Erin Howe**: Role of Rab11b-Mediated Endosomal Recycling during Brain Metastatic Outgrowth

**Tia Jarvis**: Synthavidin Self-Assembly using Unsymmetric Squaraine Dyes

**Charlotte Kunkler**: Relative Stability of DNA-DNA•RNA Base Triples

**Tyson Lager**: Aberrant Cell Surface Expression of GRP78 in Breast Cancer Cells Marks a Stem-Like Population that has Increased Metastatic Potential In Vivo

**Stefanie Lewis**: Detailed In-Situ Characterization of Uraninite from North American Deposits using a Combined FIB-SEM Approach

**Shikang Liu**: What do our Social Networks Tell us about our Health-Related Behaviors?

**Sarah Lum**: Battling the Rape Kit Backlog

**Phillip J. McCown**: Characterization of the Human RNA Methyltransferase METTL16

**Rachel Miller**: Development of a Portable Biosensor for Detection of Hormones in Technology Limited Settings

**Kristopher Murray**: Developing an In Vitro Assay to Clarify the Autotransporter Outer Membrane Secretion Mechanism

**Suzanne Neidhart**: Is Thermal Conductance of Gold Nanoparticles Influenced by Particle Shape?

**Yingjia Ni**: Functional Genome-Wide Screening Identifies Triple-Negative Breast Cancer Cell Cycle-dependent Vulnerability Driven by Genomic Gain of Death Effector Domain-Containing Protein

**Albert Olszewski**: Lower Limb Control and Joint Stability in Subjects with ISCI during Stand-to-Sit Maneuvers

**Julia R. Prince-Buitenhuys**: Dietary Ethnogenesis? An Examination of Dietary Patterns at the Santa Clara Valley Medical Center Potter's Field, California

**Craig Reingold**: Extracting Statistical Properties of Rare Earth Isotopes using the Oslo Method

**Cristal Reyna**: Quantitative N-Terminal Footprinting of Pathogenic Mycobacteria Reveals Differential N-Terminal Protein Acetylation

**Katherine Richards**: Cancer-Associated Fibroblast Exosomes Regulate Survival and Proliferation of Pancreatic Cancer Cells

**Agnieszka Ruszkowska**: Structural Insights into the RNA Methyltransferase Domain of METTL16

**Kevin Sanchez**: WhiB6 Regulation of ESX-1 Gene Expression is Controlled by a Negative Feedback Loop in *Mycobacterium marinum*

**Jessica Schiltz**: Additive Manufacturing of Materials for Wear-Resistance Applications

**Scott Shaw**: High Expression of Integrin αvβ3 Enables Uptake of RGD-Peptide Targeted Far-Red Squaraine Dyes into OVCAR-4 Cells and Tumors

**Angela M. Silski**: C—H...O Hydrogen Bonding in Pentamers of Isatin

**Madeline Smith**: Development of a Paper Analytical Device for Detecting Chemotherapy Drugs (chemoPAD)

**Tyler Spano**: Deposit Type Normalized Rare Earth Element Signatures for Nuclear Forensic Applications

**Casey Stefanski**: Loss of APC Mediates Doxorubicin Chemoresistance in Breast Cancer

**Michael Torcivia**: Lunar Sample 60025: A Story of Multiple Lithologies

**Yueh-Fu O. Wu**: Does Stringent Selection Boost or Reduce the Rate of Evolutionary Adaptation?

**Bin Xu**: Modeling the Dynamics of Cdc42 Oscillation in Fission Yeast

**Amanda Yamasaki**: Reprogramming Leukemic Cells Reveals Potential for Disease Modeling and Therapeutic Development

# AFTERNOON PODIUM SESSIONS (1:30-3:50pm – 101 & 105 Jordan)

**Jordan 101** (moderator: Susan Coiner-Collier)

1:30 – **Jamison Jangula**: Differential Roles of Calcium Signaling Channels on Epithelial Tissue Morphogenesis and Homeostasis

1:50 – **Catherine Flanley**: Population Genetics Analysis of *Phlebotomus papatasi* Sand Flies from North Africa and Middle East Regions Based on Mitochondrial Cytochrome b Haplotypes

2:10 – **Oyekola Oyekole**: A Second-Order in Time Approximation of Fluid-Structure Interaction Problem

2:30 – **Abby (Tianyuan) Cao**: In Situ Chemical Characterization of the Motile to Sessile Transition of *Pseudomonas aeruginosa* Communities

2:50 – **Ann Zeleniak**: Loss of MTSS1 Results in Increased Metastatic Potential in Pancreatic Cancer

3:10 – **Tyler Curtis**: Spectral Computed Tomography: Quantitative Anatomical Imaging

3:30 – **Susan Coiner-Collier**: Dietary Food Mechanical Properties Influence Chewing Behavior in Primates

**Jordan 105** (moderator: Tyvette Hilliard)

1:30 – **Ek Adhikari**: Influence of Oxygen or Water Vapor in a Plasma Jet and its Environment on DNA Damage

1:50 – **Tracie McGinnity**: Immunotargeted Au NPs for Radiographic Imaging of HER2+ Breast Cancer Cells

2:10 – **Tuphan Devkota**: Brillouin Oscillations from Single Au Nanoplate Opto-Acoustic Transducers

2:30 – **Andrew Schranck**: Teasing Apart Urine to Improve Advanced Wastewater Treatment and Resource Recovery

2:50 – **Junyeol Kim**: Effects of Environmental Parameters on the Protein Corona of TiO2 Nanoparticles in the Presence of Natural Organic Matter

3:10 – **Hannah Corman**: Development of Novel Anti-Leishmania Chemotherapeutics: High-Throughput Screening and Investigation of Structure-Activity Relationships of Heteroaromatic Scaffolds

3:30 – **Marwa Asem**: The Role of Wnt5a Signaling Pathway in Epithelial Ovarian Cancer Progression

# ABSTRACTS

**(alphabetical by presenter)**

**Oral Presentation:**

## Influence of Oxygen or Water Vapor in a Plasma Jet and its Environment on DNA Damage

Ek Adhikari, College of Science, Physics, Vladimir Samara, College of Science, Physics, Sylwia Ptasinska, University of Notre Dame, College of Science, Dept. of Physics

Since environmental conditions such as room temperature and humidity fluctuate arbitrarily, effects of atmospheric pressure plasma jets (APPJs) for the medical applications operating at various places and time might vary. To overcome the irreproducibility in plasma clinical performance, it is essential to maintain a stable environment around the plasma jet. To create a controlled environment for the plasma jet, a helium APPJ was enclosed in a cylindrical glass chamber filled with the pure nitrogen gas along with a fraction of oxygen or water vapor at ambient pressure. By adjusting the fraction of oxygen and water vapor in the plasma jet environment and the feed gas, a type and an amount of reactive species in the plasma jet can be changed. The plasma jet was used to induce damage in aqueous DNA at various experimental conditions. The fraction of damaged DNA and undamaged DNA were quantified using agarose gel electrophoresis. We obtained an optimal amount of oxygen or water vapor in the plasma jet environment, as well as in the feed gas, which significantly increased the level of DNA damage.

**Poster Presentation:**

## Integrative Platform for the Investigation and Modeling of the Subcellular Changes of Single Cells during Metastatic Mechanical Arrest in the Brain Vasculature

Wendy Alvarez Barrios, College of Science, Zhangli Peng, Aerospace and Mechanical Engineering, Danny Chen, Computer Science and Engineering, Lin Yang, College of Engineering, Huijie Lu, College of Engineering, Melinda Lake, Department of Mechanical and Aerospace Engineering, Ohio State University, David Hoelzle, Department of Mechanical and Aerospace Engineering, Ohio State University, Siyuan Zhang, University of Notre Dame, College of Science, Dept. of Biological Sciences

During metastasis of breast cancer, tumor cells dissociate from the primary tumor, disseminate through the vasculature, and colonize secondary organs such as the brain, lungs, liver and bones. Mechanical arrest of circulating tumor cells (CTCs) in capillary beds is an essential step in the metastatic cascade for the successful early colonization of secondary organs. During mechanical arrest, tumor cells are subjected to extreme physical stresses such as shear stress and spatial constraint exerted by blood flow, and compression from the constricting capillary on the restricted cell. These mechanical stresses may critically impact metastatic success. However, the precise physical and mechanical response of the disseminated tumor cells at the time of arrest in the vasculature to the forces of spatial constraint and shear stress remain largely unknown. Here we present an integrative platform that combines the use of a microfluidic device and computational model as a tunable system to reliably reproduce the mechanical arrest of single cells and quantitatively determine their physical response to precisely controlled mechanical stress. Using confocal microscopy and computational modeling, we found that during mechanical arrest, single tumor cells undergo extreme morphological deformations. Furthermore, the cell morphology is dependent on the magnitude of shear stress applied; with magnitudes above 60Pa inducing elongation, blebbing, and rupture of the cell membrane. Our results demonstrate that our integrative platform is a viable model system for the qualitative and quantitative study of physical cell behavior precisely at the metastatic stage of mechanical arrest. Particularly, our results highlight the direct influence of physical forces on the restricted tumor cell, and suggest the importance of these external cues as dynamic determinants of cellular processes and ultimately of metastatic success. We anticipate our platform to be a starting point for future studies seeking to understand the reciprocal molecular and biophysical interplay imposed by mechanical forces at the stage of mechanical arrest in metastasis.

**Poster Presentation:**

## Differential Proteomics Study of Fetal Bovine Serum using CZE-MS/MS

Emily Ann Amenson-Lamar, Zhenbin Zhang, Norman Dovichi, College of Science, Department of Chemistry and Biochemistry, University of Notre Dame

In recent years, there has been a crisis in reproducibility of cell culture studies. This crisis stems from variability in the components used in cell culture experiments, specifically in the serum used. Studies of human serum proteins show a wide dynamic range in the concentration of proteins, from an overwhelming amount of albumin to slight amounts of growth factors. In a study by Chan et al., 90% of the total protein content was made up of only 10 proteins; of the remaining content, 9% consisted of 12 proteins, with the remaining 1% containing proteins that were potentially important biomarkers.1 Studies of fetal bovine serum (FBS) show similar results, and form the motivation for our experiments.

In this project, we aim to elucidate the proteomic differences between different bottles, lots, and vendors of FBS. The low abundance proteins are of special concern, as many of these could influence biological processes that take place in the growth of new cells. Therefore, our sample preparation includes albumin depletion using a dye affinity column. Following this step, the samples will be digested via trypsin, labeled for quantitation, and fractionated prior to analysis. Analysis will be run using CZE-ESI-MS/MS. A multisegment injection method will be used to minimize the dead time between runs and increase the throughput of samples. The samples will be run using a data-dependent top-N method followed by more targeted MRM studies. Identifications and quantifications for each of the samples will be run for comparison. The samples will also be run via LC-MS for comparison of the analysis modes.

(1) Chan, K. C.; Lucas, D. A.; Hise, D.; Schaefer, C. F.; Xiao, Z.; Janini, G. M.; Buetow, K. H.; Issaq, H. J.; Veenstra, T. D.; Conrads, T. P. Clin. Proteomics 2004, 1, 101–226.

**Oral Presentation:**

## The Role of Wnt5a Signaling Pathway in Epithelial Ovarian Cancer Progression

Marwa Asem[1-3], Allison Young[3], Carlysa Oyama[3], Rebecca Burkhalter[3], Steven Buechler[4], Daniel L. Miller[5] and M. Sharon Stack[1-3], [1]Department of Chemistry and Biochemistry, [2]Integrated Biomedical Sciences Program, [3]Harper Cancer Research Institute, [4]Department of Applied and Computational Mathematics and Statistics, College of Science, University of Notre Dame, [5]Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD

Ovarian Cancer (OvCa) is the most fatal gynecological malignancy and the 5th leading cause of cancer death among U.S. women. The majority of women with OvCa (75%) have a very low survival rate (30%), as OvCa is usually diagnosed in late stages after development of intra-peritoneal metastasis. Thus, it is indispensable to understand the molecular mechanisms that contribute to OvCa metastatic success, in order to design effective treatment strategies to improve the overall survival of women with OvCa. Wnt5a is a non-canonical Wnt ligand that binds to several cell membrane receptors and activates many downstream signaling pathways that are fundamental for normal developmental processes during embryogenesis. In the past decade, the aberrant activation or inhibition of Wnt5a signaling is emerging as an important event in cancer progression, exerting both oncogenic and tumor suppressive effects. The role of Wnt5a in OvCa is controversial, as studies report conflicting data. In addition, mechanistic data regarding the contribution of Wnt5a to OvCa progression are largely unavailable. The main aim of this research is to obtain a molecular level understanding of Wnt5a signaling in OvCa and to investigate its potential roles in influencing OvCa metastatic success. Our data show Wnt5a is prevalent in ascites samples from women in different stages with OvCa, suggesting a role for Wnt5a in promoting disease progression. Data obtained from TCGA (n=583) show high expression of Wnt5a in primary ovarian tumors. Furthermore, Wnt5a enhanced OvCa cells adhesion, migration and invasion in a panel of organotypic and ex vivo functional assays. This was combined with striking morphological changes characteristic of an invasive phenotype in OvCa cells treated with recombinant Wnt5a protein and formation of tunneling nanotubes (TNT). Overall, our data suggests that Wnt5a plays an oncogenic role in epithelial ovarian cancer cells. More experiments exploring Wnt5a activated pathways and effects in epithelial ovarian cancer cells are underway.

**Poster Presentation:**

## What Moderately Volatile Elements in Lunar Basalts Reveal about the Moon's History

David Burney, College of Engineering, Environmental Geosciences, Clive Neal, Dept. of Civil Engineering and Geological Sciences, College of Engineering, University of Notre Dame

Moderately volatile elements (MVEs) are valuable geologic tracers of high-temperature events that occur during planetary formation, but are robust enough to not be reduced to below detection limit abundances in most geologic samples. The recent discovery of volatile compounds (H2O, S, Cl, & F) in lunar material has brought a re-evaluation of the Moon-forming "Giant Impact", as well as the high-temperature behavior of planetary forming materials. Volatiles in a planetary body dictates the geologic behavior of any magmas present, in addition to being key components (fuel, O2, & H2O) in future human planetary exploration. Issues with measuring the MVEs include: 1) They are present in very low abundance, and require a high-resolution instrument to be quantified. 2) The MVEs are susceptible to interferences from other more abundant elements present within the sample, which can artificially inflate the concentration of certain MVEs. To mitigate #1, a high-resolution inductively coupled plasma mass spectrometer was chosen for its broad chemical spectra during a single analysis, as well as its high-resolution capabilities. For #2, a series of solutions were designed to quantify, and subsequently remove the interference signal on each MVE of interest which provides a more accurate interference corrected concentration. The work presented here is the details of the method developed to quantify MVEs in lunar whole rock samples, as well as the results of 67 lunar basalt samples, 4 lunar meteorites, and 9 Martian meteorites. This geochemical data-set is the largest suite of planetary samples analyzed using the same method to allow scientific interpretation without inter-laboratory bias. The results presented here show a holistic view of not only the Earth-Moon system, but a glimpse of Mars as well. The data for the lunar samples indicates the Moon experienced a major degassing event early in its history.

**Oral Presentation:**

## In Situ Chemical Characterization of the Motile to Sessile Transition of *Pseudomonas aeruginosa* Communities

Tianyuan Cao, College of Science, Chemistry, Kristen Kramer, College of Science, Nydia Morales-Soto, Nameera F. Baig, Joshua Shrout, University of Notre Dame, Depts. of Biological Sciences and Civil Engineering and Geological Sciences, Paul Bohn, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

*Pseudomonas aeruginosa* is a Gram-negative opportunistic pathogen which infects more than 50,000 people each year in the United States alone. The ability of this organism to move, colonize surfaces, and develop biofilms that are highly resistant to antimicrobial treatment is due to its ability to readily adapt to the environment. One type of motility employed by *P. aeruginosa* to explore and colonize surfaces is swarming motility, a pre-biofilm stage where bacterial cells undergo physical and metabolic alterations. While this surface motility behavior has been studied by many groups, interest has largely remained at the biological cell level and less is known about the community-wide chemical composition, especially as it relates to the transition between the motile and sessile biofilm stages. Here we apply confocal Raman microscopy (CRM) to examine the chemical characteristics of *P. aeruginosa* wild-type PA14 (a virulent strain isolated from a burn wound) under conditions that promote swarming motility as well as multiple stages of biofilm development.

The comparison between the chemical compositions of *P. aeruginosa* swarming and biofilm samples reveals community specific chemical profiles, as well as molecules linked to the motile to sessile transition. Established swarm colonies and biofilms, both produce the alkyl-quinolone known as the *Pseudomonas* quinolone signal (PQS). However, only N-oxides (4-hydroxy-2-heptylquinoline-N-oxide, 2-nonyl-4-hydroxyquinoline, etc.) are present earlier in swarm colonies. Moreover, a closer investigation spanning from the center to the edge of a swarm colony shows high abundance of PQS at the center while N-oxides dominate the edge of the colony. Our results provide insights into the chemical changes occurring during the motile to sessile (swarm to biofilm) transition in *P. aeruginosa*, and demonstrate the broad utility of CRM for fast, accurate, non-invasive and untargeted biomolecular imaging.

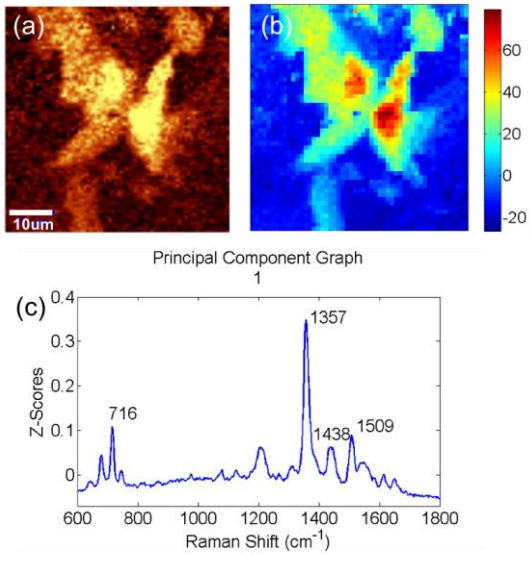



***Figure 1.*** Analysis of 24hr swarming assays of PA14. Raman image intergrated over 1330-1380 $cm^{-1}$ for representative regions of signal molecules (a); principal component heat map (b); Raman spectral loading plot (c).

**Poster Presentation:**

## Exploring the Role of the Multi-Functional Cysteine Protease SpeB in Cardiac Tissue during Group A Streptococcal Infection

Katelyn Carothers, College of Science, Shaun Lee, University of Notre Dame, College of Science, Dept. of Biological Sciences

*Streptococcus pyogenes*, also known as Group A Strep (GAS), is a species of Gram-positive bacteria and a common colonizer of human skin and mucosal surfaces. GAS is the causative agent of common and self-limiting minor infections such as pharyngitis ("strep throat"), as well as more severe infections such as necrotizing fasciitis and toxic shock. GAS infection can cause heart damage, either through chronic inflammation and autoimmune complications in rheumatic heart disease, or acute invasive infection resulting in cardiomyopathy. Despite the high mortality associated with both acute and chronic heart damage, heart tissue is understudied in GAS pathogenesis, and the contributions of specific GAS virulence factors to cell signaling and inflammatory pathways in heart tissue have not been thoroughly studied. GAS produces a large array of virulence factors that contribute to its ability to survive in the host, cause disease, and invade deeper tissue. The focus of our work is streptococcal pyrogenic exotoxin B (SpeB), a cysteine protease with multiple roles in GAS pathogenesis. SpeB is known to degrade a wide range of GAS and host proteins, but its role in pathogenesis remains controversial and appears highly dependent on the site and type of infection. Using wild-type and speB-knockout GAS strains, we have utilized a cytokine array based approach to examine differential signaling in cardiomyocytes in response to SpeB production. Subsequent biochemical analysis will allow us to determine more specifically the inflammatory signaling pathways activated in cardiomyocytes by SpeB during the course of GAS infection.

**Poster Presentation:**

## Episodic Hybrid Advantage Keeps Species Boundaries Low in Oaks

Warren Chatwin, Jeanne Romero-Severson, University of Notre Dame, College of Science, Dept. of Biological Sciences

Background: Permeable species boundaries are common within the order Fagales (oaks, chestnuts, beeches, hickories, walnuts, hazels and birches), suggesting that interspecific hybridization has adaptive value. We hypothesize that some hybrid individuals have novel allelic combinations that may enable survival during severe abiotic stress. We also propose that this effect is strongest during the long juvenile period of the life cycle, when forest trees are most vulnerable.

Methods: Species pairs are the sympatric Q. *macrocarpa-Q. bicolor* and the allopatric *Q. robur-Q. bicolor*. Hybrids were the naturally pollinated progeny of *Q.* X *warei* (*Q. robur* X *Q. bicolor*) and *Q.* X *schuettii* (*Q. bicolor* X *Q. macrocarpa*). At age two, after breaking dormancy, 500 parentage-known progeny of each hybrid type and 80-100 seedlings of each parent species were moved into a greenhouse. Half of the seedlings were subjected to four consecutive weeks of intense drought (no water), while the other half was well watered. Leaf count, height, pot weight, and survival were measured every two weeks for all individuals. One leaf/individual was saved for sequencing.

Results: Survival rates in the controls were 97-100%. For drought-stressed trees, apparent survival rates were 13% for *Q. bicolor*, 13% for *Q. robur*, 20% for *Q. macrocarpa*, 16% for progeny of *Q.* X *schuettii* and 33% for progeny of *Q.* X *warei*. The high survival rate of the progeny of *Q.* X *warei* is remarkable because neither parent species is drought tolerant. Surviving progeny from both hybrid types had a wide range of leaf counts and heights. We preliminarily conclude that some hybrids do as well as or much better than their parental species under drought stress and that this survival may be the result of many different genetic combinations. Statistical analysis of all of the phenotypic data is in progress and reduced representation sequencing of all parents and hybrids is planned.

**Poster Presentation:**

## Negative Regulation of ESX-1 Secretion by EspF is Mediated by N-Terminal Acetylation

Alexandra Chirakos, College of Science, Matthew Champion, Dept. of Chemistry and Biochemistry, Patricia Champion, College of Science, Dept. of Biological Sciences, University of Notre Dame

ESX-1 secretion system is a main virulence determinant of Mycobacterium tuberculosis, the causative agent of tuberculosis. The ESX-1 system is also conserved in non-tuberculous mycobacterial pathogens, including Mycobacterium marinum. N-terminal acetylation is the addition of an acetyl group to the N-terminus of a polypeptide chain by an N-terminal Acetyltransferase. Our work has demonstrated that ~8% of the mycobacterial proteome is N-terminally acetylated, including many ESX-1 secreted substrates. The function of N-terminal acetylation is unknown. EspF is a known ESX-1 substrate, and is required for virulence in pathogenic mycobacteria. We previously demonstrated that EspF is N-terminally acetylated. How EspF promotes virulence is unknown. To this end, we used genetics and mass spectrometry to interrogate the role of EspF, and N-terminal acetylation, in ESX-1 secretion. Our data thus far demonstrates that EspF functions as a negative regulator of ESX-1 secretion. N-terminal acetylation of EspF is important for the regulatory function of EspF. This is the first evidence of a regulatory role for EspF in ESX-1 secretion, and may lead to better understanding of how N-terminal acetylation can impact mycobacterial virulence.

**Oral Presentation:**

## Dietary Food Mechanical Properties Influence Chewing Behavior in Primates

Susan Coiner-Collier, Biological Sciences, Hui Ding, College of Science, Natalie Howe, Mendoza College of Business, Gabriela Portmann, College of Science, Science Business, Annika Fling, College of Science, Matthew J. Ravosa, University of Notre Dame, Colleges of Science and Engineering, Dept. of Biological Sciences and Aerospace and Mechanical Engineering

Repetitive loading is often invoked as potential driver of craniofacial morphology in hominins and other primates, but the dietary underpinnings of this behavior are not well understood. Food mechanical properties (FMPs), including toughness and elastic modulus, are known to influence certain aspects of primate feeding behavior, such as food selection. However, the exact role of FMPs in modulating masticatory patterns is unknown. Bone formation is regulated by high-magnitude stresses and/or cyclical loads, but there are few behavioral data on the dietary inputs generating different chewing patterns. It is consequently difficult to infer the respective roles of maximum versus repetitive loads in the development and evolution of the masticatory apparatus. We tested the hypothesis that FMPs influence three key aspects of primate mastication: chewing frequency, chewing investment, and chewing duration. We sought to establish a link between FMPs and variations in chewing behavior by performing observational feeding experiments with captive primates from 21 species. Adults were provided with five food items of known FMPs. The subsequent feeding bouts were recorded with a high-speed camcorder, and video footage was analyzed to quantify chewing behavior. We performed intra- and inter-specific analyses to compare chewing parameters with FMPs and fragmentation indices. Our results suggested that elastic modulus, rather than toughness, may be the determining factor in cyclical loading, potentially modulated by molar shearing crest height. Across species, chewing investment and duration increased in response to higher values for elastic modulus. This research has important implications for our understanding of ecomorphology and dietary adaptations in hominins and other mammals.

**Poster Presentation:**

## Chemical Characterization of Altered and Unaltered Uraninites from various Geological Settings

Loretta Corcoran, Timothy Gunther, College of Engineering, Civil Engineering, Maloney Foster, College of Science, Peter Burns, Chemistry and Biochemistry and Civil Engineering and Geological Sciences, Tyler Spano, College of Engineering, Stefanie Lewis, College of Engineering, Corinne Dorais, College of Engineering, Antonio Simonetti, University of Notre Dame, College of Engineering, Dept. of Civil Engineering and Geological Sciences

The major and trace element concentrations of a global suite of unaltered uraninite samples from five distinct deposit types; sandstone, intrusive, unconformity, vein, and metamorphic have been characterized. The spatial distribution and concentrations of major and trace elements were qualitatively determined by X-ray fluorescence (XRF) and subsequently quantified by electron microprobe analysis (EMP). The concentration of rare earth elements (REEs) and other trace elements, which are potentially significant depending on the deposit type (e.g. W, Bi, and Mo) were examined by laser ablation-inductively coupled plasma mass spectrometry (LA-ICP-MS). Following the chemical fingerprinting of the unaltered uraninite samples, a set of altered uraninites from the same locations were analyzed employing the same methods. The comparison of altered and unaltered uraninites from the same location allows for the evaluation of major and trace element mobility under various environmental conditions, such as oxidation state, over geological time. This study may provide valuable insights into the potential behavior of elements during the aging and corrosion of uranium oxide concentrate in nuclear fuel pellets and hence applicable for nuclear forensic investigations.

**Oral Presentation:**

## Development of Novel Anti-Leishmania Chemotherapeutics: High-Throughput Screening and Investigation of Structure-Activity Relationships of Heteroaromatic Scaffolds

Hannah Corman[1], Douglas A. Shoue[1], Brianna Norris-Mullins[1], Bruce J. Melancon[2], Mary Ann McDowell[1], Miguel Morales[1], Eck Institute for Global Health, College of Science, University of Notre Dame[1], Department of Chemistry and Biochemistry, University of Notre Dame[2]

The high toxicity associated with the current anti-leishmanial therapies, rampant increase of resistance, and the absence of a vaccine that is safe and effective in humans, demand the identification of new anti-leishmanials. We utilized fluorometric high-throughput screening (HTS) of small molecule libraries followed by combinatorial chemistry to identify new lead scaffolds to address this need. Primary screening of 10,000 compounds from the DIVERset-EXP library (Chembridge), was performed against axenic *L. donovani* amastigotes constitutively expressing the red fluorescent protein mCherry. Active compounds moved on to a secondary screening against intracellular *L. donovani* and *L. major* amastigotes in the human THP-1 macrophage cell line, and finally an *in vivo* murine model of cutaneous leishmaniasis (CL) was used to identify lead scaffolds. One hundred and sixteen compounds had an effectiveness greater than 90% of the 50μM miltefosine response; 61 exhibited effectiveness equal to that of 50μM miltefosine. Three scaffolds were represented multiple times in the 'hit' compounds from the preliminary screen, one such scaffold was the 2,4-diaminoquinazoline (2,4-DAQ). Active compounds that exhibited $EC_{50}$s in the less than 10μM range, were selected for secondary screening. Twenty-six (26) of the 2,4-DAQs assessed in secondary screening exhibited $EC_{50}$s between 1-10μM against axenic *L. donovani* amastigotes with selectivity indices ranging from 1-122. One of two 2,4-DAQ compounds tested in our *in vivo* imaging CL model was as effective as antimony tartrate. Comprehensive analyses of SAR of all active scaffolds is ongoing utilizing medicinal chemistry for enhanced efficacy and selectivity as well as optimal adsorption, distribution, metabolic and excretion (ADME) profiles. Utilization of this robust high-throughput platform allows for identification of novel anti-leishmanial compounds. These compounds are both potent and selective, with efficacy in an *in vivo* CL model. Future studies will test activity of these compounds in a visceral leishmaniasis model.

**Poster Presentation:**

## KREEPy Moon Rocks: KREEP Basalt Petrogenesis

Karl Cronberger, College of Engineering, Environmental Geosciences, Clive Neal, University of Notre Dame, College of Engineering, Dept. of Civil Engineering and Geological Sciences

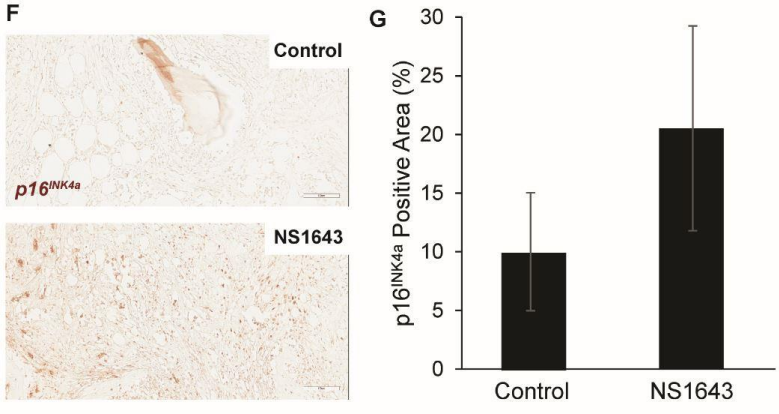
KREEP is a chemical component found on the Moon and is thought to be derived from the remains of the last liquid dregs of the lunar magma ocean. Named for the abundance of Potassium (K), Rare Earth Elements (REE), and Phosphorus (P), it is enriched in all incompatible trace elements (ITE) and has been found at every sample return mission location on the Moon. 'Pure' KREEP is not found in the sample collection, and the least diluted form of KREEP is found in the KREEP basalts. Two hypotheses purport to explain how KREEP basalt formed, one proposes that they are pristine endogenous melts of the lunar interior, and the other proposes that they formed by the impact-induced mixing of KREEP rich lithologies with Mg-rich ones. By using a variety of tools, (petrographic microscopy, crystal size distributions, X-ray element mapping, and in situ techniques such as electron probe microanalysis, and Laser Ablation Inductively Coupled Plasma Spectrometry) we evaluate the petrographic history of lunar KREEP basalts. Using trace element analyses of pyroxenes, three distinct groups of equilibrium liquids are calculated for KREEP basalts. 1) highly enriched or "Uber"-KREEP, is enriched in the LREE relative to high-K KREEP and possesses super-chondritic Zr/Hf ratios and the sub chondritic HFSE/LREE ratios, and are likely to have formed first. 2) High-K KREEP-like pyroxene-equilibrium liquids, possess chondritic to super-chondritic Zr/Hf and HFSE/LREE ratios, and derived from a variety of pyroxene compositions. 3) LREE-depleted pyroxene-equilibrium liquids, possess sub-chondritic to super-chondritic Zr/Hf ratios and sub- chondritic to super-chondritic HFSE/LREE ratios. Several models were produced to model the ITE elements within different samples. An orthopyroxenite source region underwent several stages of partial melting producing melts of decreasing ITE enrichment. These melts then mixed with each other, in varying amounts to reproduce the trace element signatures seen in the KREEP basalts. No one melting and mixing regime could explain all the observed KREEP basalt samples, implying that KREEP basalts may come from a hybrid source or from a variety of sources through magma mixing.

**Poster Presentation:**

## Effects of NS1643 on Senescence in Human Breast Cancer Metastases to Trabecular Bone

Kimberly Curtis, College of Engineering, Laurie Littlepage, Dept. of Chemistry and Biochemistry, Ricardo RomeroMoreno, College of Science, Saverio Gentile, Dept. of Molecular Pharmacology and Therapeutics, Loyola University, Lukas Nystrom, Loyola Medical Center, Glen Niebur, University of Notre Dame, College of Engineering, Dept. of Aerospace and Mechanical Engineering

The skeleton is the most common target for tumor metastasis, and more than 70% of patients who die of breast cancer have bone metastases. High morbidity is associated with bone metastasis due to its invasion of the hematopoietic marrow that can expose other organs to the cancer. Expression of voltage-gated hERG1 potassium channel changes during the cell cycle, regulating tumor cell proliferation. Inhibition of hERG1 can lead to apoptosis in leukemia cells, yet hERG1 antagonists are correlated to cardiac arrhythmias making them difficult to clinically implement. Our collaborators at Loyola University demonstrated that activating hERG1 potassium channel with the well characterized NS1643 molecule induced senescence in human mammary gland adenocarcinoma in mice. However, the effects of NS1643 on human breast cancer metastases in bone has not been studied. The objective of this study was to determine the effects of hERG1 potassium channel activator NS1643 on tumor cell senescence in human breast cancer metastases to trabecular bone. A human femoral head was obtained from Loyola Medical Center from a 59 year old female patient undergoing total hip arthroplasty due to ER+ breast cancer metastases (IRB 15-04-2500). Eight trabecular bone explants containing breast cancer metastases were excised from the human femoral head. Explants were cultured 5 days in a custom bioreactor. At the end of culture, explants were scanned on the μCT to observe bone architecture, fixed in 10% formalin for 24 hours, decalcified in 10% EDTA, processed, and embedded in paraffin. Tissue was sliced into 5 μm sections, and mounted on microscope slides for histology. Sections were stained for H&E and pankeratin to identify tumor cells. Tissue sections were also stained for p16INK4a to quantify senescent cells. Histology showed disorganized bone and the presence of tumor cells in all explants. Trabecular explants treated with NS1643 did not demonstrate significantly increased protein expression of senescence marker p16INK4a in the marrow, however, there was a trend toward increased senescence. A larger sample size is necessary to fully determine the effectiveness of NS1643 in promoting tumor senescence in human bone.



**Oral Presentation:**

## Spectral Computed Tomography: Quantitative Anatomical Imaging

Tyler Curtis, College of Engineering, Tracie McGinnity, College of Engineering, Prakash Nallathamby, Aerospace and Mechanical Engineering, Ryan Roeder, University of Notre Dame, College of Engineering, Dept. of Aerospace and Mechanical Engineering

X-ray computed tomography (CT) is widely used for clinical diagnostics providing high resolution images at relatively low cost. However, CT only provides relative attenuation of tissues and contrast agents limiting its quantitative efficacy. Recent advances in photon-counting detectors have enabled quantitative anatomical imaging of tissues and contrast agents greatly broadening potential applications. Using a commercially available photon counting spectral CT (MARS Bioimaging) several applications were demonstrated using contrast agents and tissue substitutes. Multi-agent (k-edge) imaging and quantitative molecular imaging with spectral CT was demonstrated using a clinical agent (iodine) and a proposed spectral library of contrast agents (Gd2O3, HfO2, and Au) comprising core-shell nanoparticles (NPs). Spectral CT enabled simultaneous color delineation and quantitative molecular imaging of each contrast agent, with a spatial resolution of ~300 μm. Accurate quantitative multi-material decomposition was enabled by energy-dependent differences in the X-ray attenuation of each material. Importantly, accurate spatial and quantitative identification of co-localized contrast agents was verified using mixed compositions of contrast agents (iodine and Gd2O3, 0-20 mM) and tissue (CaCl2, 0-580 mM), (AUC > .95, RMSE < 12% maximum concentration). Qualitative preliminary results have also shown feasible delineation between compositions of calcium and phosphoric acid, enabling identification of calcium compositions associated with various disease pathologies (e.g. calcium phosphate and calcium oxalate breast microcalcifications). These results indicate that spectral CT can be widely applicable for quantitative diagnostic imaging without the use of contrast agents in hard tissue disease pathologies and in combination with ligand targeted nanoparticle contrast agents for soft tissue pathologies.

**Oral Presentation:**

**Brillouin Oscillations from Single Au Nanoplate Opto-Acoustic Transducers**

Tuphan Devkota, College of Science, Chemistry, Gary Beane, Chemistry and Biochemistry, Kuai Yu, College of Electronic Science and Technology, Shenzhen University, Shenzhen 518060, P. R. China, Guo Ping Wang, College of Electronic Science and Technology, Shenzhen University, Shenzhen 518060, P. R. China, Gregory Hartland, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

Brillouin oscillations are GHz frequency waves that arise from the interaction of light with acoustic waves. The frequency of these oscillations depends on the refractive index and speed of sound of the material. Thus Brillouin oscillations measurements provide a way of differentiating different types of materials, and have recently been used in imaging applications. In this study, Brillouin oscillations are observed through ultrafast transient reflectivity measurements using chemically synthesized Au nanoplates as opto-acoustic transducers. The Au nanoplates are semi-transparent, which allows the Brillouin oscillations to be observed from material on both sides of the plate. The measured frequencies are consistent with the values expected from the speeds of sound in the different materials, however, the attenuation constants are much larger than those reported in previous studies. The increased damping is attributed to the diffraction of the acoustic wave as it propagates away from the excitation region. These results are important for understanding the relationship between frequency and spatial resolution in Brillouin oscillation microscopy.

**Poster Presentation:**

## Identification of an N-Acetyl Transferase from *Mycobacterium marinum* with Activity towards the Virulence Factor EsxA (ESAT-6)

Micah Ferrell, College of Science, Biological Sciences, Matthew Champion, Chemistry and Biochemistry, Patricia Champion, University of Notre Dame, College of Science, Dept. of Biological Sciences

To successfully establish intracellular infections pathogenic mycobacteria must secrete multiple small protein virulence factors. A subset of these proteins are translocated by the ESX-1 export system. Disruption of this system leads to attenuation. Proteomic studies have revealed that many of these virulence factors are N-terminally acetylated, a modification hitherto believed to be rare in prokaryotes. Both the significance of acetylation in pathogenesis and the mechanism by which it is achieved remain unknown. We sought to identify the N-acetyl transferase (NAT) enzymes responsible for acetylating virulence factor N-termini. To identify specific NAT-virulence factor relationships we have developed an in vitro expression screen to test peptides derived from virulence factor N-termini. We tested 14 NATs from the opportunistic human pathogen *Mycobacterium marinum* with a peptide from EsxA (ESAT-6) with mass spectrometry to detect acetylation. We identified two enzymes which generated acetylated peptides. Both NATs were further expressed, purified and assayed for activity by colorimetric assay confirming the initial screening results. Finally, purified enzymes were evaluated for activity towards N-terminal peptides from two other virulence factors to determine acetylation specificity. We have identified the product of a previously uncharacterized gene as a NAT enzyme with activity towards EsxA and no detectable activity towards other peptides tested. These results indicate the validity of the in vitro expression screen as a means to identify NAT-substrate relationships for further characterization.

**Oral Presentation:**

## Population Genetics Analysis of *Phlebotomus papatasi* Sand Flies from North Africa and Middle East Regions Based on Mitochondrial *Cytochrome b* Haplotypes

Catherine M. Flanley, College of Science, Biological Sciences, University of Notre Dame, Omar Hamarsheh, Al-Quds University, Gwen Stayback, University of Notre Dame, Mariha Wadsworth, University of Notre Dame, Douglas A. Shoue, University of Notre Dame, Mehmet Karakus, Ege University, Mohammad Reza Yaghoobi-Ershadi, Tehran University of Medical Sciences, Andreas Kruger, Bundeswehr Hospital Hamburg, Mary Ann McDowell, University of Notre Dame, College of Science, Biological Sciences

The *Phlebotomus papatasi* sand fly is a vector of cutaneous leishmaniasis (CL) over a widespread geographic range. Population genetics is a valuable tool in understanding the level of genetic variability present in vector populations, vector competence, and the development of novel control strategies. This study elucidated the genetic differentiation between *P. papatasi* populations in Egypt and Jordan that inhabit distinct ecotopes and compared this structure to *P. papatasi* populations from a broader geographical range. The mtDNA *cytochrome b* gene was amplified and sequenced from 116 individual sand flies from Aswan and North Sinai, Egypt, as well as Swaymeh and Malka, Jordan. Haplotypes were identified and used to generate a median-joining network, $F_{ST}$ values, and isolation-by-distance were evaluated. Additional sand fly individuals from Afghanistan, Iran, Israel, Jordan, Libya, Tunisia, and Turkey were included as well as previously published haplotypes to provide a robust genetic variation analysis. Thirteen haplotypes were identified with nine variant sites from the Egypt and Jordan. No unique haplotypes were identified from samples in North Sinai, Egypt, two were observed in Aswan, Egypt, four from Swaymeh, Jordan, and two in Malka, Jordan. The Jordan populations clustered separately from the Egypt populations and produced more unique haplotypes than Egypt. Pairwise $F_{ST}$ values fall in the range 0.024-0.648 and indicate a strong differentiation between Egypt and Jordan populations, although this population structure is not due to isolation-by-distance. Other factors, such as environmental influences and the genetic variability in the circulating *L. major* parasites, may contribute significantly to this heterogeneity. The present study aligns with previous reports in that genetic differentiation exists between the populations of this widely dispersed species but overall, the species remains relatively homogeneous.

**Poster Presentation:**

## Fractalkine Receptor Downregulation in Heterogeneous Brain Metastasis-Associated Myeloid Cells Induces Tumor-Promoting Interferon Response

Ian Guldner, College of Science, Biological Sciences, Abigail Brunory, College of Science, Matthew McGoldrick, College of Science, Biological Sciences and English, Jeanne Farnan, College of Science, Martin Barron, College of Science, Zhuo Zhao, College of Engineering, Yizhe Zhang, College of Engineering, Longhua Sun, Biological Sciences, Lin Yang, College of Engineering, Qingfei Wang, Biological Sciences, Danny Chen, Computer Science and Engineering, Jun Li, Applied and Computational Mathematics and Statistics, Samuel Brady, Biomedical Informatics, Siyuan Zhang, University of Notre Dame, College of Science, Dept. of Biological Sciences

Myeloid cells are heterogeneous cells that mediate the innate immune response through cytokine secretion and phagocytosis. While targeting Ccr2+ inflammatory myeloid cells has been exploited as a potential anti-tumor therapy, the dynamic interplay between pro- and anti-inflammatory myeloid subpopulations during tumor progression and their role in regulating metastasis remains controversial. Particularly, the myeloid response and contribution to brain metastasis, an incurable malignancy in an immunologically-unique organ fortified by the blood-brain-barrier, has yet to be fully revealed. Here, we demonstrated that genetic cellular depletion of fractalkine receptor-positive (Cx3cr1+) myeloid cells significantly reduced brain metastases, suggesting an overall pro-metastatic role of Cx3cr1+ myeloid cells. Interestingly, genetic perturbation of specific myeloid cell subsets demonstrated divergent roles of these subpopulations in regulating brain metastasis: the brain-specific Cx3cr1highCcr2- myeloid population (microglia) is anti-tumorigenic while the peripherally-derived Cx3cr1lowCcr2+ myeloid subset does not affect brain metastasis. To dissect the molecular underpinnings of brain metastasis-associated myeloid cells, we performed single cell RNA sequencing (scRNA-seq) on myeloid cells derived from metastasis-burdened brains. scRNA-seq revealed significant heterogeneity within the brain myeloid population and transcriptionally distinct myeloid subsets with wide-ranging functions including cytolytic activity, antigen presentation, and immune suppression. Interestingly, Cx3cr1, a key regulator of microglia homeostatic function, was downregulated in myeloid cells during brain metastasis. Furthermore, genetic ablation of Cx3cr1 in myeloid cells resulted in increased brain metastasis burden. Mechanistically, scRNA-seq of Cx3cr1-deficient myeloid cells revealed that loss of Cx3cr1 results in increased expression of pro-inflammatory genes, especially those related to interferon signaling. Finally, treatment with minocycline, an FDA-approved antibiotic that ameliorates interferon signaling, reduced myeloid hyperactivation, resulting in reduced brain metastasis burden. Together, our multi-pronged approach revealed context-dependent heterogeneity and plasticity of the brain myeloid response during brain metastasis. Our proof-of-concept study provides a new avenue to prevent aggressive brain metastasis outgrowth by targeting neuroinflammation.

**Poster Presentation:**

## Calcium and Iron Isotope Analysis of Uraninite and Other Uranium-Rich Materials: Development of Potential New Forensic Isotope Tracer Methods

Timothy Gunther, College of Engineering, Civil Engineering, Peter Burns, Chemistry and Biochemistry and Civil Engineering and Geological Sciences, Loretta Corcoran, College of Engineering, Antonio Simonetti, University of Notre Dame, College of Engineering, Dept. of Civil Engineering and Geological Sciences

Employing methods that aid in tracking down illicit nuclear materials, such as uraninite (UO2) or uranium ore concentrate (UOC), are of utmost importance in forensic analyses for source attribution purposes. Natural uranium ores and UOCs are part of the early stages of the nuclear fuel cycle and constitute commonly intercepted materials. Consequently, there is a need to better understand and document the forensic signatures of different ore types such that an origin can be determined for seized illicit nuclear materials. Recently, several studies have successfully attributed uranium ores and UOCs to specific mining/geographic areas based on trace element abundances (e.g., rare earth elements-REEs) and isotopic (Sr, U) fingerprinting. Uranium ore and UOCs are also known to contain a myriad of trace elements that persist as impurities through the enrichment process, such as aluminum, calcium, potassium among others. Moreover, natural uraninite is commonly associated with secondary Ca- and Fe-rich alteration zones/phases that are characterized by variable REE contents. Hence, this study represents a first-time investigation of the Ca and Fe isotope signatures of natural uraninite and its associated alteration products, with the primary objectives being three-fold: 1- Establish baseline Ca and Fe isotopic signatures for U deposits worldwide; 2- Better understand the physical conditions (temperature, redox) involved with uraninite formation and its subsequent alteration; and 3- Determine the feasibility of Ca and/or Fe isotope measurements as forensic signatures of nuclear materials for source attribution purposes.

**Poster Presentation:**

## Aging Promotes Changes to Peritoneal and Omental Collagen Structure that Contribute to Increased Ovarian Cancer Metastatic Success

Elizabeth Harper[1,4], Elizabeth Loughran[1,4], Annemarie Leonard[1], Ryan Phan[1], Tyvette Hilliard[1], Marwa Asem[1,4], Yueying Liu[1], Jing Yang[1], Yuliya Klymenko,[2] Jeff Johnson[1], Emma Sheedy[3], Laura Tarwater[1], Zonggao Shi[1], Matthew Leevy,[2] Matthew J. Ravosa[2] and M. Sharon Stack[1]
[1]Department of Chemistry & Biochemistry, [2]Department of Biological Sciences, [3]Department of Mathematics, [4]Integrated Biomedical Sciences Graduate Program, Harper Cancer Research Institute, University of Notre Dame, Notre Dame, IN

Ovarian cancer (OvCa) is the deadliest cancer of the female reproductive system, ranking fifth in overall cancer deaths among women. Unlike the majority of cancers, OvCa metastasizes via diffusion through the peritoneal cavity, resulting in multiple metastatic sites, including the omentum and peritoneum. These metastasizing OvCa cells induce rapid mesothelial cell retraction and readily adhere to the sub-mesothelial collagen of the extracellular matrix. Epidemiologic data identifies age as a significant risk factor in OvCa, as about half of diagnoses are in women over the age of 63. Despite this, age is understudied in the OvCa field. Using a C57Bl/6 mouse model of aging, young (Y) mice ranging from 3-6 months of age, and aged (A) mice ranging from 20-23 months of age, corresponding to women aged 20-30 years (Y) and 60-67 years (A) were used to study the role aging has on metastasis. Fluorescently tagged C57Bl/6 syngeneic ID8 $p53^{-/-}$ mouse OvCa surface epithelial cells were injected intraperitoneally in young and aged mice and disease progression was evaluated for 5.5 weeks. Organ-specific tumor burden was quantified with ImageJ, revealing increased tumor burden in aged mice compared to their young counterparts. These results were reproduced in the FVB mouse model using syngeneic $PTEN^{shRNA}/KRAS^{G12V}$ modified FVB OvCa oviductal epithelial cells. Second Harmonic Generation Microscopy (SHG) was used to visualize collagen of the peritoneal and omental tissues from young and aged C57Bl/6 mice. Distinct structural differences were shown in omental collagen in the Y vs A cohorts and validated with Scanning Electron Microscopy (SEM). Additionally, Nanoindentation illustrated mechanical differences between young and aged peritoneal samples. In conclusion, aging induces changes in the structure and mechanical strength of peritoneal and omental collagen, which contribute to OvCa metastasis.

**Poster Presentation:**

## Mesothelin Expression Impacts the Metastatic Success of Ovarian Cancer

Tyvette Hilliard (1, 2), Kyle Iwamoto (3), Elizabeth Loughran (1,2,4), Marwa Asem (1,2), Yueying Liu (2), Jing Yang(2), Laura Tarwater(2), Yuliya Klymenko (2,5), Jeff Johnson (2), Zonggao Shi (1,2), Gifty Marfowaa (6), Brooke Kowalski (1), Madeleine G Yemc (7), Phillip Petrasko (7) and M. Sharon Stack (1, 2)
(1) Department of Chemistry and Biochemistry, (2) Harper Cancer Research Institute, (3) Department of Chemical and Biomolecular Engineering, (4) Integrated Biomedical Sciences Graduate Program, (5) Department of Biological Sciences, (6) Department of Pre-professional Studies, (7) Department of Science Business, College of Science, University of Notre Dame

Ovarian cancer is the most lethal gynecological cancer in U.S. women due to presentation of most women, at diagnosis, with advanced stage disease with widely disseminated intraperitoneal metastasis. Metastasizing tumor cells grow rapidly and aggressively attach to the mesothelium of organs within the peritoneal cavity producing secondary lesions. Mesothelin (MSLN), a glycoprotein that is over expressed in many cancers is suggested to play a role in tumor progression and adherence. However, the biological function of MSLN is not fully understood as MSLN knockout mice do not present with an abnormal phenotype. Conversely, MSLN has been shown to bind to the ovarian cancer antigen, CA-125, and thought to play a role in the peritoneal diffusion of ovarian tumor cells. Taking into consideration the potential importance of MSLN/CA-125 binding in ovarian tumor metastasis within the peritoneum, MSLN wild type (WT) and knockout (KO) mice were used to explore the role of mesothelin on the susceptibility of ovarian tumor cells adherence to the mesothelium of the intraperitoneal organs. An allograft tumor study, using MSLN WT and KO mice injected intraperitoneally with fluorescently-tagged syngeneic murine ovarian cancer cells was performed. Disease progression was evaluated post injection by fluorescent in vivo imaging prior to end point dissection. Abdominal organs were dissected, imaged, and organ-specific tumor burden was quantified. Notably, tumor burden was significantly decreased in the omentum of MSLN KO mice compared to WT mice. The results demonstrate a loss of mesothelial cell-ovarian tumor cell adhesion in the peritoneal cavity of mice devoid of MSLN.

**Poster Presentation:**

## Kinematic Analysis of Lunge Characteristics in Young, Healthy Subjects

Simon Hinnekens, James Schmiedeler, College of Engineering, Aerospace and Mechanical Engineering, University of Notre Dame

Current improvements in biomedical research and biomechanics have considerably changed our understanding of the human body. While muscular reinforcement and rehabilitation were previously done exclusively by physiotherapy, we can now call on biomechanics models and simulations to work in the same way. Either in high-level sports, where we can evaluate muscle strength and advise for reinforcement, or in medicine and rehabilitation, where we can find weaknesses in muscles or tendons and prevent injuries, physiotherapy and biomechanics are being increasingly combined. Resources are still limited, however, as current motion capture systems are slow due to the time for placing markers and performing calibration. In the Locomotion and Biomechanics Lab at Notre Dame, a markerless motion capture and data analysis system from DARI Motion reduces the time required for experiment and facilitates analysis of a large corpus of data. Current work is focused on the study of the contralateral hip extension during lunge motions. The sample group consists of more than 1200 subjects (19.7 ± 1.2 years of age). Maximum knee flexion angle, maximum hip flexion angle and maximum ankle flexion angle are used for comparison with previous results from literature. For lunges, subjects were asked to step as far as they could and to lunge as deep as they could, which results in motions that have not been previously reported in the literature. Some correlation in the distribution of the hip and knee angles was found, however, while the ankle angle presents a more disperse distribution. In contrast to some other rehabilitation motion results (squats), no correlation between BMI and gender was found for lunges, but there is a significant difference for gender alone.

**Poster Presentation:**

## A Series of Iron Carbenes and their Unique Reactivity with Styrene

Melissa Hoffbauer, College of Science, Vlad Iluc, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

The diphosphine ligand [PCH 2 P] = ([PCH 2 P] = (bis[2-(diisopropylphosphino)phenyl]methane) was attached to an iron metal center via transmetalation of [{PC(sp 3 )HP}Li(THF)] with FeCl 2 (PMe 3 ) 2. Subsequent metathesis with MeLi generated [{PC(sp 3 )HP}FeMe], which could be treated with either benzonitrile or pivalonitrile to induce the elimination of methane and yield the corresponding carbene complexes, [{PC(sp 2 )P}Fe(NCPh) 2 ] and [{PC(sp 2 )P}Fe(NC t Bu)(N 2 )], respectively. Through a ligand substitution with trimethylphosphine, [{PC(sp 2 )P}Fe(NC t Bu)(N 2 )] was converted to [{PC(sp 2 )P}Fe(PMe 3 )(N 2 )]. The reactivity of the PMe 3 carbene complex towards styrene was investigated, and results displayed unique reactivity. Thus, the oxidized derivatives, [{PC(sp 2 )P}Fe(PMe 3 )(I)] and [{PC(sp 2 )P}FeI 2 )], were synthesized and their reactivity with styrene studied.

**Poster Presentation:**

## Role of Rab11b-Mediated Endosomal Recycling during Brain Metastatic Outgrowth

Erin Howe, College of Science, Jeremiah Zartman, College of Engineering, Chemical and Biomolecular Engineering, Xuejuan Tan, Biological Sciences, Miranda Burnette, Patricia Schnepp, College of Science, Siyuan Zhang, University of Notre Dame, College of Science, Dept. of Biological Sciences

Breast cancer brain metastases are an urgent clinical problem, accounting for 30% of breast cancer mortality. Tragically, as targeted therapies provide better control of localized and systemic disease, women who respond to initial treatment ultimately develop brain metastases, and no clinically approved drug shows promising efficacy for brain metastases. It is well established that communication with the metastatic microenvironment is critical for metastatic success, but the exact nature of this communication is poorly understood. We hypothesize that genes up-regulated during the progression from single cells to actively proliferating brain metastases are functionally required for metastatic progression. To dissect the dynamic nature of brain metastatic progression, we performed transcriptome analysis in small tumors 7 days post injection (dpi) and overtly metastatic tumors 40 dpi. We identified 108 of the most highly up-regulated genes, and utilized a Drosophila model to screen 448 RNAi constructs for a functional role in brain metastasis. We identified Rab11 as an important mediator of brain metastatic outgrowth. Rab11 regulates vesicular transport in the endosomal and exosomal recycling pathways, and is responsible for recycling of surface proteins back to the surface. Examination of Rab11b mRNA levels in human breast cancer cells reveals that Rab11b is moderately up-regulated in primary tumors, but very strongly up-regulated in brain metastases. Indeed, brain microenvironment-mediated up-regulation of Rab11b is necessary for the formation of breast cancer brain metastasis. Interestingly, Rab11b is most highly expressed at 6 dpi, when cells have successfully adapted to the brain microenvironment and initiated metastatic outgrowth. Together, our findings indicate that breast cancer cells up-regulate Rab11b as they adapt to the brain microenvironment, and this up-regulation is required for successful progression formation of overt metastases.

**Oral Presentation:**

## Differential Roles of Calcium Signaling Channels on Epithelial Tissue Morphogenesis and Homeostasis

Jamison Jangula, Qinfeng Wu, Cody Narciso, and Jeremiah Zartman, College of Engineering, Department of Chemical and Biomolecular Engineering, University of Notre Dame

The robust formation of organs during development depends on the careful regulation of cellular processes such as cell adhesion, mechanical stiffness of the cell membrane, and internal pressure to create the three-dimensional tissue-scale architecture. A sophisticated communication system coordinates these developmental processes. Many birth defects and diseases occur when this communication system breaks down. In particular, calcium ions play critical roles in regulation of cell mechanics during organ development. However, the regulation and function of the core calcium-based signaling systems and its role in regulating tissue mechanics are still poorly understood. Here we tested a hypothesized mechanism of stress dissipation mediated by $Ca^{2+}$ during tissue development. To do so, we perturbed $Ca^{2+}$ concentrations in cells genetically through perturbation of $IP_3R$ channels, which control flux of $Ca^{2+}$ from endoplasmic reticulum stores into the cell cytoplasm and SERCA channels, which remove $Ca^{2+}$ from the cytoplasm into the ER. We show that both increased and decreased cytoplasmic $Ca^{2+}$ concentrations result in decreased apical E-cadherin localization and tissue shape defects in the wing disc pouch of *Drosophila melanogaster* 3rd instar larva. Furthermore, tumor-like overgrowth was observed in late stage wing discs when SERCA is inhibited. In contrast, inhibition of store operated calcium entry through Stim or Orai did not lead to the tumor-like phenotype. Together these results map specific components of the core $Ca^{2+}$ signaling toolkit to regulation of tissue morphogenesis and homeostasis.

**Poster Presentation:**

**Synthavidin Self-Assembly using Unsymmetric Squaraine Dyes**

Tia Jarvis, College of Science, Chemistry, Bradley Smith, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

Biotin/avidin self-assembly is a powerful platform for nanoscale fabrication and capture with many different applications in science, medicine, and nanotechnology. However, there are several well-recognized drawbacks to this system that limit performance in certain technical areas and there is a need for synthetic mimics that can either become superior replacements or operational partners with bio-orthogonal recognition properties. First generation squaraine dyes have exhibited nanomolar affinities towards tetralactam macrocycles but the fluorescence properties are not ideal for many imaging applications. This poster will describe second generation squaraine dyes.

**Oral Presentation:**

## Effects of Environmental Parameters on the Protein Corona of TiO2 Nanoparticles in the Presence of Natural Organic Matter

Junyeol Kim, College of Engineering, Civil Engineering, Kyle Doudrick, University of Notre Dame, College of Engineering, Dept. of Civil Engineering and Geological Sciences

Engineered nanomaterials (ENM) introduced into aquatic environments interact with macromolecules (e.g., natural organic matter and proteins) that form corona on ENM surfaces. Due to a new identity of ENM resulting from the formed corona, fate and transport studies relying on the physicochemical properties of pristine surfaces have limitations for representing accurate ENM behavior. For more accurate studies on ENM behavior considering macromolecular corona, we used time-resolved in-situ ATR-FTIR spectroscopy to investigate ENM corona formation and transformation upon environmental perturbations such as macromolecular type (e.g., oxalate and bovine serum albumin), ionic strength, ion speciation, and pH. The impact of pre-adsorbed macromolecules on the development and transformation of ENM corona was also investigated in macromolecular main and secondary structures. Additionally, adsorption dynamics of macromolecules in the presence and absence of pre-formed corona was examined using two-dimensional correlation spectroscopy. Environmental perturbations induced distinctive differences on ENM corona behavior when pre-adsorbed corona were present.

**Poster Presentation:**

## Relative Stability of DNA-DNA•RNA Base Triples

Charlotte Kunkler, College of Science, Biochemistry, Jessica Brown, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

RNA triple helices (or triplexes) were first shown to form in vitro over sixty years ago. Since then, triple helices have been identified in eukaryotic, prokaryotic, and viral RNAs, and shown to regulate transcription, to process post-transcriptional RNA, to modify chromatin, and to repair DNA. There is an emerging hypothesis that long noncoding (lnc)RNAs may regulate transcription by binding to genomic (g)DNA via a triple helix. Bioinformatic studies, which are based on the relative stability of pure DNA triple helices, suggest that there is a large population of triplex-forming motifs in the genome. Here, we investigate the relative stability of sixteen DNA-DNA•RNA pyrimidine motif base triples using electrophoretic mobility shift assays (EMSA) by varying a single common position: X-Y•Z (where X-Y = A-T, T-A, C-G, G-C and Z = U, A, C, G). Eight base triples exhibited a binding affinity within 2-fold of the canonical T-A•U base triple: C-G•C, C-G•A, G-C•U, C-G•U, G-C•C, G-C•A, G-C•G, and C-G•G. Overall, the stability of each base triple appears to be governed by the identity of the DNA Watson-Crick base pair (X-Y) rather than the identity of the RNA Hoogsteen base (Z): C-G•Z > G-C•Z > A-T•Z > T-A•Z (disregarding T-A•U). These results show that the canonical T-A•U and C-G•C base triples may not be the only pyrimidine motif base triples that support formation of a lncRNA•gDNA triple helix.

**Poster Presentation:**

## Aberrant Cell Surface Expression of GRP78 in Breast Cancer Cells Marks a Stem-Like Population that has Increased Metastatic Potential In Vivo

Tyson Lager, College of Science, Biological Sciences, Ian Guldner, College of Science, Biological Sciences, Henry Conner, Biological Sciences, Siyuan Zhang, Biological Sciences, Athanasia Panopoulos, University of Notre Dame, College of Science, Dept. of Biological Sciences

Reliable approaches to identify and target stem-cell mechanisms that mediate aggressive cancer could have great therapeutic value, based on the growing evidence of stem-like signatures in metastatic cancers. However, how to best identify and target stem-like mechanisms aberrantly utilized by cancer cells has been challenging. We harnessed the power of induced pluripotent stem cells (iPSCs) to identify embryonic mechanisms exploited by cancer. A screen comparing the cell surface proteome of iPSCs and breast cancer cells identified GRP78, a normally ER-restricted protein that is a key regulator of the stress response, but has been shown to be aberrantly expressed on the cell surface of several cancers, where it can act as a signaling molecule by poorly understood mechanisms. Without insight into the specific GRP78-dependent mechanisms that are responsible for specifically mediating aggressive cancer, it will be difficult to determine how to best target GRP78. We have discovered that (1) sGRP78 is expressed on iPSCs (but not their somatic parental populations) and plays an important role in reprogramming, (2) sGRP78 promotes cellular functions such as proliferation/survival and migration in both stem cells and breast cancer cells (3) overexpression of GRP78 in breast cancer cells leads to an induction of a previously established CD24-/CD44+ 'cancer stem cell' (CSC) population (4) sGRP78+ breast cancer cell populations are enriched for stem-like genes and appear to be a subset of previously established CSCs (5) sGRP78+ breast cancer cell populations show a significantly enhanced ability to seed metastatic organ sites in vivo (6) GRP78 interacts with Dermcidin (DCD) at the cell surface of cancer cells and iPSCs, where it is important in regulating stem cell and cancer cell migration and survival/proliferation. These collective findings suggest that sGRP78 marks a stem-like population in breast cancer cells that has increased metastatic potential in vivo, and that sGRP78 and DCD cooperate to regulate key cellular functions mediating this metastatic seeding advantage. Overall, this work has implications for understanding how cancer cells exploit stem cell mechanisms, which could provide novel strategies for chemotherapeutic targeting of aggressive stem-like breast cancer cell populations.

**Poster Presentation:**

## Detailed In-Situ Characterization of Uraninite from North American Deposits using a Combined FIB-SEM Approach

Stefanie Lewis, College of Engineering, Peter Burns, Chemistry and Biochemistry and Civil Engineering and Geological Sciences, Tyler Spano, College of Engineering, Loretta Corcoran, Civil Engineering and Geological Sciences, Antonio Simonetti, University of Notre Dame, College of Engineering, Dept. of Civil Engineering and Geological Sciences

Focused ion beam (FIB) coupled with scanning electron microscopy (SEM) in situ analyses were conducted on natural uraninites from various North American deposits to further understand their complex chemical heterogeneity. The uraninite samples are first investigated using electron microprobe (EMP) analysis to determine their major element compositions. From the EMP analyses, one major element is selected for use as an internal standard, which is then employed for data reduction of laser ablation-inductively coupled plasma mass spectrometry (LA-ICP-MS) analyses to produce trace element concentrations. It was determined that selecting different major elements for the internal standard unexpectedly yielded trace element concentrations that varied by several orders of magnitude for the same LA-ICP-MS analysis spot. To better understand this unexpected result, combined FIB and SEM analyses were performed to obtain a 3-dimensional distribution of the trace elements within the uraninite samples investigated. One possible explanation for the contrasting elemental abundances may be due to the presence of sub-micrometer to nanometer-sized inclusions within uraninite, which are more easily sampled by the LA-ICP-MS setup due to the larger volume (30 µm spot) employed for analysis compared to that used for the EMP investigations (<5 µm beam). Hence, we propose using a combined micro-analytical approach involving elemental maps obtained via micro-XRF, and FIB and SEM in-depth profiling, which will provide valuable insights into the best methodology for obtaining accurate trace element abundances of uraninite at high spatial resolution.

**Poster Presentation:**

**What do our Social Networks Tell us about our Health-Related Behaviors?**

Shikang Liu, College of Engineering, Christian Poellabauer, Computer Science and Engineering, Aaron Striegel, Omar Lizardo, Sociology, David Hachen, Sociology, Tijana Milenkovic, University of Notre Dame, College of Engineering, Dept. of Computer Science and Engineering

Social communication data related to phone calls, SMS, Facebook interactions, etc. have become popular in studies of social networks. These studies have covered various aspects, encompassing the evolution of network structures, the relationship between different communication types, and the relationship between social networks and personality traits. A popular research direction has been to understand the impact of social networks on health. For example, the spread of obesity or smoking in social networks has been studied through quantitative analysis. The initial studies of the relationship between social networks and health dealt with analyses of static network data, while recent efforts have exploited the wealth of dynamic network data that has become available with the popularity of mobile devices such as cell phones. For instance, by clustering students that have similar evolving social network positions, and by comparing the resulting network-based clusters with the users' trait-based clusters, a number of network-trait relationships were detected and validated. With the popularity of highly capable and inexpensive wearable sensors, a wealth of dynamic user trait data can be collected easily. In particular, wearable sensors that collect health-related user traits have become very popular, such as FitBit devices. Hence, by integrating analyses of dynamic social network data with analyses of dynamic health-related trait data, one can study the link between social networks and health more accurately. To our knowledge, no one has done this yet. We address this gap as follows. Our analysis consists of the following major steps: 1) How to construct a dynamic network from raw temporal user communication (e.g., SMS) events? 2) What does global network analysis reveal in terms of the network structure (e.g., degree distribution)? 3) What does local network analysis reveal in terms of the relationship between users' evolving social network positions and evolving health-related behaviors?

We study longitudinal data from the NetHealth study in which the smartphone usage and health-related behaviors of around 700 college students are monitored for over two years. We systematically construct and analyze the dynamic social network. In addition, we identify users whose evolving social network positions correlate with his/her health-related behaviors.

**Poster Presentation:**

## Battling the Rape Kit Backlog

Sarah Lum, College of Science, Norman Dovichi, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

The national backlog in sexual assault cases is estimated to be between tens of thousands to a half million untested rape kits. Current methods are time and labor intensive, requiring overnight procedures and delivering a lower than 40% success rate. The primary challenge crime labs face in analyzing these cases is the separation of purified male DNA from the mixture of primarily female DNA from gynecological swabs. Effective elution of the sample from the swab and efficient separation of intact sperm cells from epithelial and other cellular debris allow for a successful analysis of the perpetrator DNA. Capillary zone electrophoresis (CZE) is a promising tool to perform the cell separation and has three major advantages over alternative technologies: a small amount of sample is consumed, which allows for replicate analyses of limited available evidence; rapid separation time compared to standard methods; and single cell detection and collection when interfaced with an automated fraction collector developed in-house. In this work, simulated sexual assault samples are eluted from cotton swabs and the mixture is directly electrokinetically injected into a novel CZE system where intact cells and lysed cellular matrices are separated by their unique electrophoretic properties. Sample eluted from the distal end of the capillary is collected into individual wells on a microtiter plate which correspond to a CZE migration time interval. Light microscopy is used to confirm the separation and collection of intact sperm cells at designated time points for further downstream analysis.

**Poster Presentation:**

## Characterization of the Human RNA Methyltransferase METTL16

Phillip J. McCown and Jessica A. Brown, College of Science, University of Notre Dame, Dept. of Chemistry and Biochemistry

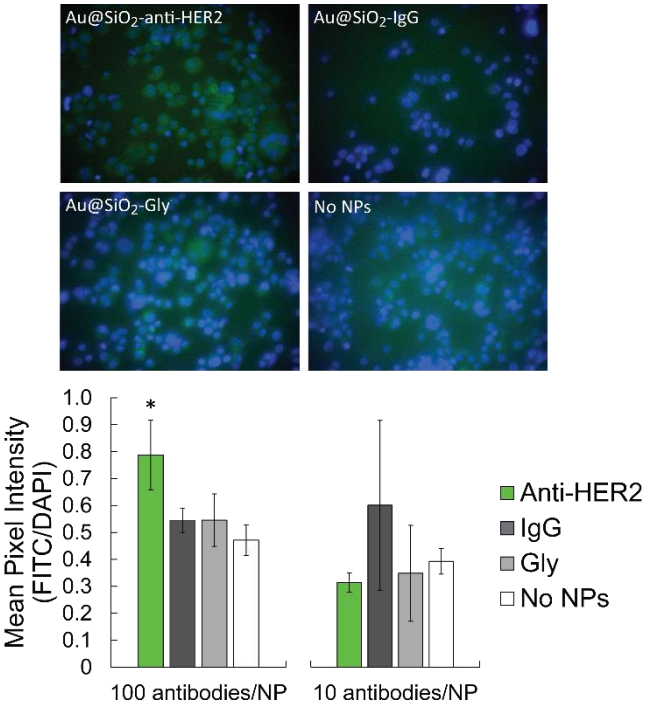
RNA transcripts undergo chemical modifications throughout the entire life of the transcript. One such RNA modification, N6-methyladenosine (m6A), is involved in human development, cancer, and other diseases such as diabetes. While many m6A RNA modifications are made by the methyltransferase-like protein 3/14 (METTL3/METTL14) complex, METTL16 has emerged as a newly established participant in m6A biology. We examined the expression and subcellular localization of METTL16 in cells from cancer patients and Miller-Dieker Syndrome (MDS). Previous immunofluorescence studies in HeLa cells show that METTL16 localizes predominantly to the nucleus while immunohistochemistry of METTL16 in melanoma, colorectal adenocarcinoma, invasive ductal carcinoma of the breast, glioma, and pancreatic ductal adenocarcinoma biopsies shows that its localization can occur outside of the nucleus. Western blot analysis confirms that METTL16 is expressed in A549, MCF-7, BJ, and two MDS cell lines, GM06047 and GM06097. Further, METTL16 in MCF-7, BJ, GM06047, and GM06097 cells may form a tight dimer. By studying the localization and expression of METTL16, we hope to elucidate the roles of METTL16 as an m6A RNA methyltransferase in cancer and human biology.

**Oral Presentation:**

## Immunotargeted Au NPs for Radiographic Imaging of HER2+ Breast Cancer Cells

Tracie McGinnity, College of Engineering, Aerospace and Mechanical Engineering, Tracy Vargo-Gogola, Biological Sciences, College of Science, Ryan Roeder, University of Notre Dame, College of Engineering, Dept. of Aerospace and Mechanical Engineering

Epidermal growth factor 2 receptor (HER2) is overexpressed in 20-25% of breast cancers. Trastuzumab (anti-HER2), a clinically approved monoclonal antibody, suppresses tumor growth by targeting the HER2 receptor and has been clinically successful in the treatment of HER2+ breast cancers. Gold nanoparticles (Au NPs) conjugated with anti-HER2 antibodies have shown promise for radiographic imaging of HER2+ cells and tumors. However, the effect of the number of anti-HER2 antibodies on the surface of NPs remains unknown. Therefore, the objective of this study was to investigate immunotargeting, cellular uptake, and radiographic imaging of HER2+ breast cancer cells with Au@SiO2 core-shell NPs bioconjugated with varying surface density of anti-HER2. Au@SiO2 core-shell NPs were volume-loaded with FITC in the SiO2 shell for combined fluorescence imaging and conjugated with Herceptin (trastuzumab, Au@SiO2-anti-HER2), immunoglobulin G (Au@SiO2-IgG), and glycine (Au@SiO2-Gly) to provide positive, isotype, and negative controls, respectively. The number of antibodies conjugated to Au NP surfaces was controlled by varying the Au NP concentration at a constant antibody concentration. Au@SiO2-anti-HER2 and Au@SiO2-IgG NPs exhibited strong binding to protein A biobeads verifying antibody conjugation. HER2+ breast cancer cells (SKBR3, ATCC) were incubated with 2 μM Au@SiO2-anti-HER2, Au@SiO2-IgG, and Au@SiO2-Gly NPs for 8 h. NP targeting to cells was measured by fluorescence microscopy using the calibrated FITC signal to determine the concentration of Au NPs which targeted cells. Au@SiO2-anti-HER2 NPs conjugated with ~100 antibodies/NP exhibited immunotargeting for HER2+ cells evidenced by significantly greater fluorescence compared with the non-targeted control groups lacking receptor-specific binding (Fig. 1). Interestingly, Au@SiO2-anti-HER2 NPs conjugated with ~10 antibodies/NP did not exhibit immunotargeting for HER2+ cells evidenced by similar fluorescence for all NP groups. Therefore, immunotargeting HER2+ breast cancer cells with Au@SiO2-anti-HER2 NPs was dependent on the number of antibodies/NP.



**Poster Presentation:**

## Development of a Portable Biosensor for Detection of Hormones in Technology Limited Settings

Rachel Miller, College of Science, Chemistry and Biochemistry, Marya Lieberman, Chemistry and Biochemistry, Abigail Weaver, College of Science, Biochemistry, Holly Goodson, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

There is a growing need for analytical tools in technology-limited environments in multiple fields. When trying to regulate pharmaceutical composition or environmental contamination, public safety depends on the ability to accurately detect whether these regulations are being met. However, technology, trained personnel, and laboratory infrastructure provide a barrier for reliable analytical detection in low-resource settings, such as low- and middle-income countries (LMIC) or remote test sites. Drugs containing biological molecules, such as contraceptives, are among the long list of medications that are being counterfeit in the US and around the world (up to 30% of drugs are counterfeit in LMIC). Moreover, increased pharmaceutical use and production has led to the contamination of lakes and streams with endocrine disrupting compounds. Thus, there is an urgent need to develop a field-friendly device for the detection of bioactive analytes. The goal of this project is to develop a field-friendly way to detect estrogen and other hormones based on a paper-based, whole-cell yeast biosensor technology previously developed by our lab. Our original biosensor can detect tetracycline antibiotics over a range of 30 to 10,000 ug/mL. The long shelf life, durability, and ease of use makes this device well-suited for technology limiting environments. This device is being expanded in order to detect estrogen and modified to include new reporters. Thus far, we have created a fluorescence-based estrogen biosensor capable of detecting estrogen concentrations as low as 0.5 nM E2 and are currently working to integrate it into a paper-based test.

**Poster Presentation:**

## Developing an In Vitro Assay to Clarify the Autotransporter Outer Membrane Secretion Mechanism

Kristopher Murray, College of Science, Biochemistry, Esther Braselmann, Patricia Clark, University of Notre Dame, Colleges of Science and Engineering, Dept. of Chemical and Biomolecular Engineering and Chemistry and Biochemistry

The autotransporter (AT, also known as Type Va) secretion pathway is the simplest and most widely used mechanism to secrete virulence proteins to the surface of Gram-negative bacteria. ATs contain three functional components: an N-terminal signal sequence that directs export across the inner membrane into the periplasm, a central 'passenger' domain that will become the mature virulence protein after secretion out of the cell, and a C-terminal β-barrel 'translocator' domain that inserts into the outer membrane (OM) before the passenger is exported into the extracellular space. OM translocation occurs in the absence of ATP or a proton gradient. The 'autotransporter' moniker is based on an early model that these monomeric proteins contain all required elements for OM translocation, but recent studies have concluded that other periplasmic factors, including molecular chaperones and the β-barrel assembly machinery (BAM) complex, contribute to translocation. The BAM complex assists in the folding β-barrel proteins into the outer membrane, but it is less clear whether it also contributes to the process of passenger export ('autotransport'). To test the independence of AT passenger export and further characterize the secretion mechanism, we have developed an in vitro vesicle assay to characterize AT translocator folding and passenger autotransport. Our results indicate the translocator folds significantly slower than the passenger, potentially blocking autotransport in vitro. These results suggest a model where the BAM complex accelerates translocator folding without directly contributing to the passenger autotransport mechanism.

**Poster Presentation:**

**Is Thermal Conductance of Gold Nanoparticles Influenced by Particle Shape?**

Suzanne Neidhart, J. Daniel Gezelter, College of Science, Dept. of Chemistry and Biochemistry, University of Notre Dame

Molecular dynamics simulations were performed to model the interfacial thermal conductance from bare gold nanoparticles into a hexane solvent. The computed conductance was found to depend not only on particle shape, but also on the size of the nanoparticles, particularly for nanospheres. These results are compared with conductance out of the planar facets, (111), (100), and (110), which are all commonly exhibited in small patches by the spherical particles. Undercoordination of the surface atoms explains some of these observations. The surface-normal vibrational densities of states were used to describe a frequency-dependent phonon transmission model, which shows a size-dependent enhancement of low-frequency coupling to the solvent.

**Poster Presentation:**

## Functional Genome-Wide Screening Identifies Triple-Negative Breast Cancer Cell Cycle-dependent Vulnerability Driven by Genomic Gain of Death Effector Domain-Containing Protein

Yingjia Ni, College of Science, Biological Sciences, Jenna Koenig, College of Science, Biological Sciences, Barnes Werner, College of Science, Biological Sciences, Laurie Littlepage, Chemistry and Biochemistry, Longhua Sun, Biological Sciences, Siyuan Zhang, University of Notre Dame, College of Science, Dept. of Biological Sciences

Triple-negative breast cancer (TNBC) has a poor prognosis. There is no FDA approved targeted therapy to 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 5,043 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) enhance 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 PDXs, regardless of RB status. Taken together, this study revealed a novel TNBC tumor vulnerability driven by genome gain of DEDD. Clinical exploiting this dysregulated cell cycle mechanism governing the sensitivity to CDK4/6 inhibitor containing combinatorial therapy provides a new avenue for clinical management of TNBC patients.

**Poster Presentation:**

## Lower Limb Control and Joint Stability in Subjects with ISCI during Stand-to-Sit Maneuvers

Albert Olszewski, College of Engineering, Mechanical Engineering, Kevin O'Brien, College of Engineering, Mechanical Engineering, D. Michele Basso, School of Health and Rehabilitation Sciences, The Ohio State University, James Schmiedeler, University of Notre Dame, College of Engineering, Dept. of Aerospace and Mechanical Engineering

Downhill treadmill training aims to rehabilitate eccentric motor control in subjects with incomplete spinal cord injury (ISCI). The purpose of this study was to characterize lower limb control deficits in kinetic, kinematic, and EMG characteristics of subjects with ISCI performing stand-to-sit maneuvers. Observations of downhill treadmill training effects were made through examination of vertical ground reaction force (vGRF), valgus knee characteristics, and EMG signals of individuals with ISCI. Most subjects with ISCI exhibited symmetrical vGRF, and downhill training did not have any significant effect on symmetry for subjects with asymmetrical vGRF. Abnormal vGRF characteristics could be a result of injury location and severity. Statistically significant deficits in valgus moments and angles were found in subjects with ISCI. Valgus moment values were not significantly affected by downhill training, but more subjects exhibited negative training effects than positive ones in a longitudinal study. Unhealthy valgus characteristics can be caused by strengthening the quadriceps and gluteus medius without strengthening of the hamstrings and gluteus maximus. It is possible that downhill training increases leg muscle activity, but not in all muscles necessary for joint stability. Prior to downhill training, subjects with ISCI had significantly lower peak EMG signals than healthy controls. In a longitudinal study, training resulted in some subjects exhibiting healthy EMG characteristics in muscles that act eccentrically during stand-to-sit after training. This suggests that downhill training does aid in the rehabilitation of eccentric motor control for some subjects with ISCI. Overall, results show that individuals with ISCI exhibit statistically significant deficits in lower limb control and eccentric muscle activation. Some subjects exhibit positive training effects in terms of eccentric muscle activation, but some subjects exhibit negative training effects in terms of valgus characteristics during stand-to-sit. Results from this study can be used to validate and further develop experimental techniques of ISCI rehabilitation.

**Oral Presentation:**

## A Second-Order in Time Approximation of Fluid-Structure Interaction Problem

Oyekola Oyekole, College of Science, Applied and Computational Mathematics and Statistics, Catalin Trenchea, Department of Mathematics, University of Pittsburgh, Pittsburgh, PA, Martina Bukac, University of Notre Dame, College of Science, Dept. of Applied and Computational Mathematics and Statistics

Fluid-structure interaction (FSI) problems arise in many applications, such as aerodynamics, geo-mechanics and biomedical engineering. They are characterized by highly non-linear coupling between two different physical phenomena. As a result, the development of robust numerical algorithms is a subject of intensive research. Since coupled FSI problems give rise to large and ill-conditioned systems of algebraic equations, partitioned methods have often been used to split the coupled problem into smaller and better-conditioned sub-problems. However, in applications where the density of the structure is comparable to the density of the fluid (such as the interaction between blood and arterial walls), classical partitioned schemes suffer from instabilities known as the *added mass effect*. In this case, the development of stable, non-iterative numerical schemes for FSI problems is challenging – even for first-order accurate solution techniques.

We propose and analyze a novel, second-order accurate in time, partitioned method for the interaction between an incompressible, viscous fluid and a thin, elastic structure. The proposed numerical method is based on the Crank-Nicolson discretization scheme, which is used to decouple the system into a fluid sub-problem and a structure sub-problem. The scheme is loosely coupled, and therefore at every time step, each sub-problem is solved only once. Energy and a priori error estimates for a fully discretized scheme using finite element spatial discretization are derived. We prove that the scheme is stable under a CFL condition, second-order convergent in time and optimally convergent in space. We also present two numerical examples that support the theoretically obtained results. Using realistic parameter values for blood flow in a human common carotid artery, our simulation results demonstrate that the proposed scheme is stable and accurate when applied to problems related to blood flow modeling.

**Poster Presentation:**

## Dietary Ethnogenesis? An Examination of Dietary Patterns at the Santa Clara Valley Medical Center Potter's Field, California

Julia R. Prince-Buitenhuys, College of Arts and Letters, Department of Anthropology, University of Notre Dame

Previous research into 19th century dietary variation within the United States has found significant variation based on social class, ancestry, and region. However, research to date has not systematically examined the specific social, cultural, and economic factors that contribute to dietary variation found throughout the United States during the 19th century. This study examines stable isotopes of carbon, nitrogen, and oxygen to examine the relationship between ethnic preferences, regional specialization, and socioeconomic status and diet among individuals interred at the Santa Clara Valley Medical Center potter's field (1870 - circa 1935). The results demonstrate that local agricultural industry and low socioeconomic status play more important roles in explaining dietary patterns than ancestry or ethnic differences at the Santa Clara Valley Medical Center. Despite cultural preferences in food preparation, the ingredients regularly consumed are often isotopically similar. This factor likely explains some of the variation observed in diet across the 19th century United States. Stable isotope analysis provides a useful tool for exploring the relationship between the development of agricultural industries and dietary patterns, and provides an avenue to research how socioeconomic status related to food choices in the 19th century United States.

**Poster Presentation:**

## Extracting Statistical Properties of Rare Earth Isotopes using the Oslo Method

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The statistical model for nuclear reactions is one of the most quantitative theories in nuclear physics. In this model, two reacting nuclei fuse to form one compound nucleus in a highly excited state. At these high excitation energies, the spacing between nuclear resonances rapidly approaches the width of the resonances. Over this quasi-continuum, nuclear reaction cross sections can be treated as averaged functions, calculated using statistical factors. These factors include the nuclear level density (NDL) and gamma-strength function (gSF).

Providing experimental constraints for the NDL and gSF for samarium and dysprosium isotopes is important to nuclear astrophysics, nuclear security, and nuclear structure. Since many reaction cross sections relevant to stellar nucleosynthesis have yet to be measured, Hauser Feshbach calculations are often employed. Furthermore, they can be used to predict photonuclear and inverse radiative-capture reaction cross sections of fission products. Constraining statistical factors is, therefore, imperative to nuclear security as well. In the field of nuclear structure, theorists predict an enhancement in the gSF at low gamma-ray energies. Experimental evidence shows that the enhancement is the result of dipole transitions, but the electromagnetic character has yet to be determined. This can be verified experimentally via observation of gamma-ray scattering in segmented detectors.

In this work, the NDL and gSF were extracted using the STARLiTeR array at Texas A&M University. STARLiTeR consists of two segmented silicon detectors to identify charged reaction products, coupled with six BGO suppressed HPGe Clover detectors to measure gamma-ray energies. Particle-gamma coincidence provide correlation matrices of excitation energy vs gamma-ray energy, for which the Oslo method is employed to simultaneously extract the NDL and gSF. The results of 152,154Sm(p,d) measurement will be presented. Future plans for measurements on other rare earth nuclei will be discussed.

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**Poster Presentation:**

## Quantitative N-Terminal Footprinting of Pathogenic Mycobacteria Reveals Differential N-Terminal Protein Acetylation

Cristal Reyna, College of Science, Biological Sciences, Matthew Champion, Chemistry and Biochemistry, Patricia Champion, University of Notre Dame, College of Science, Dept. of Biological Sciences

N-terminal acetylation (NTA) is the addition of an acetyl group at the N-terminal amine of a polypeptide. In higher organisms, NTA influences protein stability and function. NTA also occurs on bacterial proteins, but the role of NTA in bacteria remains unclear. NTA of mycobacterial proteins has been reported, with a focus on secreted virulence factors from the ESX (ESAT-6 system) systems. However, several questions remain regarding NTA in mycobacteria, including the determinants of NTA and the ratio of acetylation in specific protein populations. We sought to define and quantify the populations of N-terminally acetylated proteins in both the human pathogen *Mycobacterium tuberculosis* and the non-tuberculous opportunistic pathogen, *Mycobacterium marinum*. To this end, we took a proteomics approach, using parallel N-terminal enrichment from proteolytic digests coupled with charge based selection and stable isotope ratio mass spectrometry to enrich, identify, and quantify N-terminally acetylated proteins. We show that NTA is a diverse and abundant modification of mycobacterial proteins. Mycobacterial NTA predominantly occurs on Thr, indicating that the underlying biology of NTA in mycobacteria is unique compared to NTA in other bacteria. We isolated 142 proteins in both acetylated and unacetylated forms, indicating that homeostasis of NTA is regulated. Finally, we identified at least seven proteins which have differential acetylation ratios from cytosolic and secreted protein fractions. These findings suggest that mycobacteria either specifically promote acetylated substrates for secretion, or that the accumulation of secreted proteins is influenced by acetylation status.

**Poster Presentation:**

## Cancer-Associated Fibroblast Exosomes Regulate Survival and Proliferation of Pancreatic Cancer Cells

Katherine Richards, College of Science, Biological Sciences, Reginald Hill, University of Notre Dame, College of Science, Dept. of Biological Sciences

Cancer associated fibroblasts (CAFs) comprise the majority of the tumor bulk of pancreatic adenocarcinomas (PDACs). Current efforts to eradicate these tumors focus predominantly on targeting the proliferation of rapidly growing cancer epithelial cells. We know that this is largely ineffective with resistance arising in most tumors following exposure to chemotherapy. Despite the long-standing recognition of the prominence of CAFs in PDAC, the effect of chemotherapy on CAFs and how they may contribute to drug resistance in neighboring cancer cells is not well characterized. Here we show that CAFs exposed to chemotherapy play an active role in regulating the survival and proliferation of cancer cells. We found that CAFs are intrinsically resistant to gemcitabine, the chemotherapeutic standard of care for PDAC. Further, CAFs exposed to gemcitabine significantly increase the release of extracellular vesicles called exosomes. These exosomes increased chemoresistance-inducing factor, Snail, in recipient epithelial cells and promote proliferation and drug resistance. Finally, treatment of gemcitabine-exposed CAFs with an inhibitor of exosome release, GW4869, significantly reduces survival in co-cultured epithelial cells, signifying an important role of CAF exosomes in chemotherapeutic drug resistance. Collectively, these findings show the potential for exosome inhibitors as treatment options alongside chemotherapy for overcoming PDAC chemoresistance.

**Poster Presentation:**

## Structural Insights into the RNA Methyltransferase Domain of METTL16

Agnieszka Ruszkowska, Chemistry and Biochemistry, Milosz Ruszkowski, Synchrotron Radiation Research Section of MCL National Cancer Institute, Argonne, IL, Jessica Brown, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

N6-methyladenosine (m6A) is an RNA modification that plays a central role in biology. Most m6A marks are catalyzed by a heterodimeric complex comprised of methyltransferase-like protein 3 and methyltransferase-like protein 14 (METTL3/14), which specifically methylates adenine within a GGACU sequence motif. However, ~20% of m6A marks are added by methyltransferase-like protein 16 (METTL16), a recently confirmed m6A RNA methyltransferase. This protein has been shown to methylate the human MAT2A transcript, U6 spliceosomal small nuclear RNA, and sites enriched in introns or intron-exon boundaries. In contrast to METTL3/14, METTL16 substrate recognition is not well understood, although preliminary studies suggest METTL16 uses a combination of sequence and structure to recognize its RNA substrates. Interestingly, METTL16 also interacts with an RNA triple helix located at the 3' end of the long non-coding RNA, MALAT1 (metastasis-associated lung adenocarcinoma transcript 1). METTL16 binding depends on both the nucleotide composition and structure of the MALAT1 triple helix. Thus, our goal is to understand the structural basis of RNA recognition by METTL16, beginning with the MALAT1 triple helix.

In this study, we present two X-ray crystal structures of the N-terminal methyltransferase domain (residues 1-291) of METTL16: an apo form (1.9 Å resolution) and a complex with the S-adenosylhomocysteine (SAH) (2.1 Å resolution). As expected, the structure revealed a highly conserved Rossmann fold characteristic of SAM-dependent methyltransferases. In addition, the methyltransferase domain contains a large, positively charged groove that is likely an RNA binding site. However, native gel-shift results indicate that the N-terminal domain (1-291 aa) of METTL16 alone does not bind to the MALAT1 triple helix. This observation confirms that the interaction between METTL16 and MALAT1 is likely independent of its methyltransferase activity. Future studies will focus on mapping the RNA binding activity of METTL16 and characterizing its RNA substrate specificity in vitro.

**Poster Presentation:**

## WhiB6 Regulation of ESX-1 Gene Expression is Controlled by a Negative Feedback Loop in *Mycobacterium marinum*

Kevin Sanchez[a], Rachel E. Bosserman[a], Tiffany T. Nguyen[a], Alexandra E. Chirakos[a], Micah J. Ferrell[a], Matthew M. Champion[b], Robert B. Abramovitch[c], and Patricia A. Champion[a]; [a]College of Science, Dept. of Biological Sciences, University of Notre Dame; [b]College of Science, Dept. of Chemistry and Biochemistry, University of Notre Dame; [c]Dept. of Microbiology and Molecular Genetics, Michigan State University

ESX (ESAT-6-system) export systems play diverse roles across mycobacterial species. Interestingly, genetic disruption of ESX systems in different species does not result in an accumulation of protein substrates in the mycobacterial cell. However, the mechanisms underlying this observation are elusive. We hypothesized that the levels of ESX substrates were regulated by a feedback control mechanism, linking the levels of substrate to the secretory status of ESX systems. To test this hypothesis, we used a combination of genetic, transcriptomic, and proteomic approaches to define export-dependent mechanisms regulating the levels of ESX-1 substrates in *Mycobacterium marinum*. WhiB6 is a transcription factor that regulates expression of genes encoding ESX-1 substrates. We found that in the absence of the genes encoding conserved membrane components of the ESX-1 system, the expression of the *whiB6* gene and genes encoding ESX-1 substrates were reduced. Accordingly, the levels of ESX-1 substrates were decreased, and WhiB6 was not detected in *M. marinum* strains lacking genes encoding ESX-1 components. We demonstrated that in the absence of $EccCb_1$, a conserved ESX-1 component, substrate gene expression was restored by constitutive, but not native expression, of the *whiB6* gene. Finally, we found that the loss of WhiB6 in *M. marinum* lowered, but did not abrogate ESX-1 secretion. Together, our findings demonstrate that the levels of ESX-1 substrates in *M. marinum* are fine-tuned by negative feedback control, linking the expression of the *whiB6* gene to the status of the ESX-1 membrane complex.

**Poster Presentation:**

## Additive Manufacturing of Materials for Wear-Resistance Applications

Jessica Schiltz, Steven Schmid, University of Notre Dame, College of Engineering, Dept. of Aerospace and Mechanical Engineering

Additive manufacturing (AM) is thought to have significant potential for a wide variety of applications in aerospace, automotive and medical product industries, among others. AM is quickly becoming cost competitive for many products due to the savings associated with avoidance of tooling, reduced energy use, and conferred design flexibility. Ceramic AM processing is not as sophisticated or robust as AM polymers and metals, and wear resistance of AM-produced ceramics is relatively unknown (as are wear-resistant forms of any AM material). Three AM processes, binder jetting (BJ), stereolithography (SLA) and digital light processing (DLP), have been demonstrated with alumina, zirconia, and silicon nitride, but minimal assessments have been made to evaluate the suitability of these ceramics for functional bearings. The performance of AM ceramic materials will be evaluated using wear and strength tests. Coupon green samples are fired as appropriate, machined to establish geometry and surface finish, and then tested on a standard pin-on-disk Ortho-POD (AMTI Watertown, MA). Similarly, fracture toughness and flexural strength are critical properties to many applications, and will be measured directly with a four-point bending apparatus. The development of new wear-resistant materials with improved fracture-resistance is anticipated to stem from these evaluations.

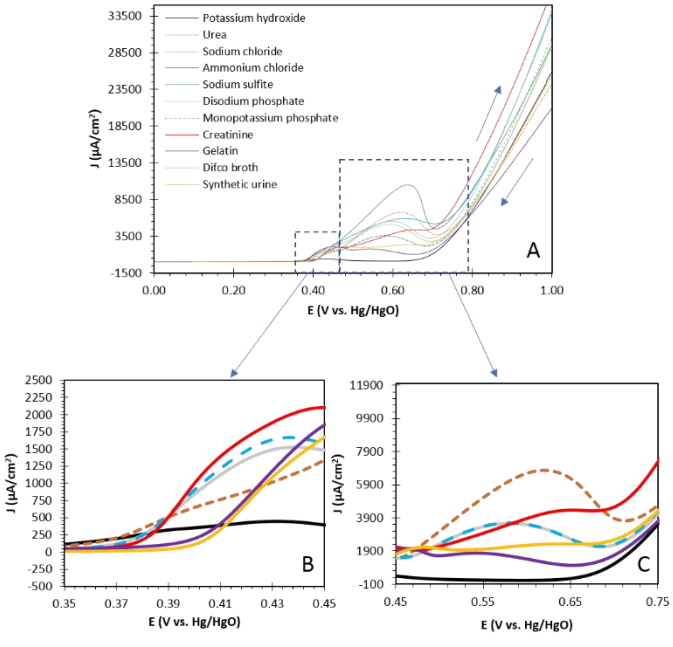
**Oral Presentation:**

## Teasing Apart Urine to Improve Advanced Wastewater Treatment and Resource Recovery

Andrew Schranck, College of Engineering, Civil Engineering, David Clark, College of Engineering, Elon Yates, College of Engineering, Civil Engineering, Randal Marks, College of Engineering, Kyle Doudrick, University of Notre Dame, College of Engineering, Dept. of Civil Engineering and Geological Sciences

In this study, we evaluated the effects of synthetic urine components such as phosphate and chloride compounds on the electrochemical performance of urea electrooxidation for source separated urine treatment technologies. Nitrogen compounds place unnecessary economic, time, and space burdens on municipal wastewater treatment processes, because they require long reactor retention times and multi-step processes to treat. Urea (CO2) is the predominant compound in urine, accounting for 80% of the nitrogen concentration in municipal wastewater yet only 1% of the total wastewater volume. Separating this nitrogenous component from the municipal wastewater stream and electrochemically transforming it into innocuous gases and valuable hydrogen gas transforms the idea of wastewater as a valueless burden and moves it into the realm of resource recovery and waste-to-value engineering. Nickel has been shown to be a cost effective, earth abundant material for electrooxidizing urea employed in alkaline conditions, but the effects of the individual urine constituents on this process need greater understanding. Comparison of nickel, cobalt, and nickel-cobalt (NiCo2O4) materials on carbon paper electrodes in cyclic voltammetry confirmed the benefit of employing cobalt with nickel for reduced oxidation onset potential and overall current density. We observed significant impairment of urea electrooxidation current density at NiCo2O4 electrodes for synthetic urine and individual components as compared to urea.

Phosphates, creatinine, and gelatin had the most detrimental impact on current density in the urea electrooxidation range from approximately 0.37-0.75 V vs. Hg/HgO reference electrode (see Figure). The binding mechanisms of these urine components, as well as those of the resulting oxidation byproducts such as CO2 and N2, with the NiCo2O4 electrode surface are critical factors to understanding how to improve the efficiency of electrochemical urine treatment. Greater understanding of these mechanisms will contribute to advancing environmental sustainability through improved wastewater treatment processing and energy efficiency.



**Poster Presentation:**

## High Expression of Integrin αvβ3 Enables Uptake of RGD-Peptide Targeted Far-Red Squaraine Dyes into OVCAR-4 Cells and Tumors

Scott Shaw, College of Science, Amanda Houser, College of Science, Felicia Roland, College of Science, Simon Padanilam, Cynthia Schreiber, College of Science, Paul Battles, Chemistry, Seamus Brennan, Chemistry, Bradley Smith, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

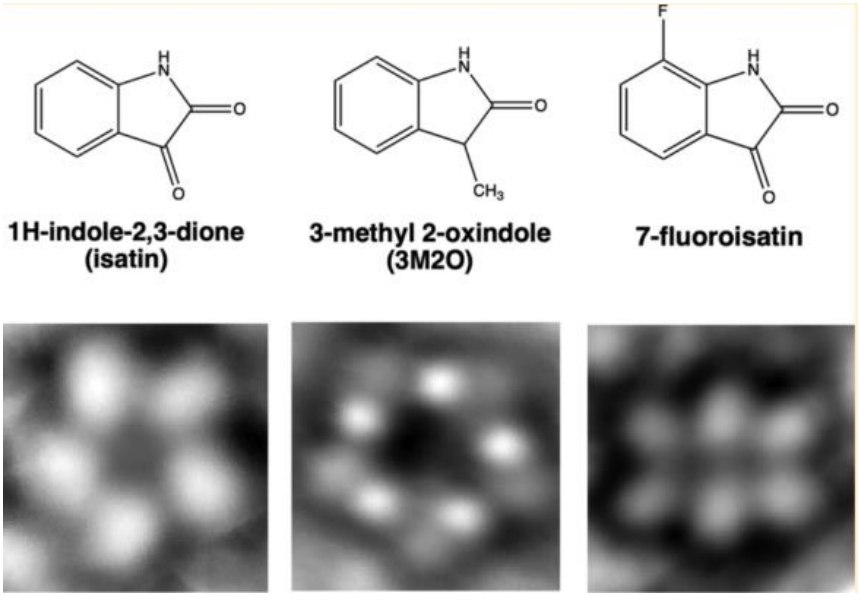
Ovarian cancer is the 5th leading cause of cancer related deaths among women in the United States, and is the most lethal gynecological disease. High-grade serous ovarian cancer (HGSOC) is responsible for approximately 80% of ovarian cancer cases and two-thirds of ovarian cancer deaths. Imaging strategies which support early detection or the surgical removal of HGSOC tissue would increase survival, but adequate model systems to study the disease remain a limiting factor in this research. The cell line OVCAR-4 was ranked as one of the most representative cell lines for HGSOC based off its genomic and other features, but little work has been done to assess the internalization of targeted imaging agents into OVCAR-4 cells and tumors. Proteome profiles suggest OVCAR-4 should be amenable to targeting strategies towards integrins. Here we describe the synthesis of molecular probes whose structures are comprised of a near-infrared fluorescent squaraine dye as a reporter covalently attached to one or two cyclic pentapeptide cRGDfK sequences for integrin targeting. We have determine the number and density of integrin αvβ3 receptors for OVCAR-4 and several control cell lines, and we measure cell uptake of the two fluorescent probes into these cells. We find that cell uptake of the divalent probe into OVCAR-4 tumors is higher relative to the monovalent probe, which is itself higher relative to an untargeted probe. We find this targeting trend is also seen in OVCAR-4 mouse tumor models. Achieving this receptor targeting using near-infrared fluorescent multivalent probes is broadly significant for two major reasons: (1) it establishes OVCAR-4 as an experimental model cell line for both in vitro and in vivo studies of HGSOC with molecular probes (2) it advances the use of RGD-targeted squaraine dyes as imaging agents for possible diagnostic applications.

**Poster Presentation:**

## C—H...O Hydrogen Bonding in Pentamers of Isatin

Angela. M. Silski[1], Ryan D. Brown[1], Jacob P. Petersen[1], Joseph Coman[1], David Turner[1], Zach M. Smith[2], John C. Poutsma[2], Steven A. Corcelli[1], S. Alex Kandel[1]; [1]Department of Chemistry and Biochemistry, College of Science, University of Notre Dame; [2]Department of Chemistry, The College of William and Mary

Molecular self-assembly is an attractive bottom-up approach to nanostructure fabrication. Controlled assembly of supramolecular structures can be realized through careful tuning of non-covalent interactions. In this study, we tune the intermolecular hydrogen bond contacts by varying molecular functionality of substituted indoles and observe their self-assembled structure via scanning tunneling microscopy (STM). Self-assembled monolayers of 1H-indole-2,3-dione (isatin), 3-methyl 2-oxindole, and 7-fluoroisatin are observed on the Au(111) surface. We observe that isatin forms pentamers, with density functional theory providing support for a cyclic structure stabilized by both N – H...O and C – H...O hydrogen bonds between neighboring molecules. The C – H...O bond is made between the 7-position C – H acting as the hydrogen bond donor and the 3-position carbonyl as the hydrogen bond acceptor, and calculations show that the isatin pentamer structure is 12 kJ/mol more stable than the dimer. When the 3-position carbonyl is removed and replaced with a methyl group (3-methyl 2-oxindole), we observe a monolayer with a mixture of catemer chains and pentameric clusters that are qualitatively different from those of isatin. Pentamer formation is completely broken when the 7-position proton is removed and replaced with fluorine; the monolayer of 7-fluoroisatin is composed of a mixture of close packed ordered domains and hexamer clusters. The role of C – H...O bonding in forming isatin pentamers is supported by electrospray ionization mass spectrometry (ESI-MS) measurements, which show a propensity for isatin cluster formation including magic-number isatin pentamers, while 3-methyl 2-oxindole and 7-fluoroisatin show relatively little clustering under the same conditions.

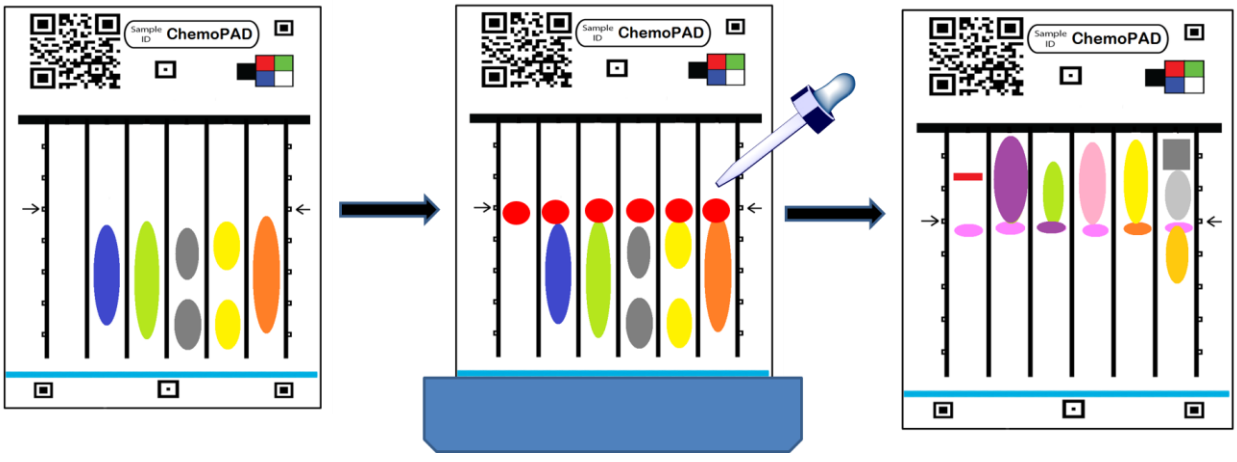


**Poster Presentation:**

## Development of a Paper Analytical Device for Detecting Chemotherapy Drugs (chemoPAD)

Madeline Smith, College of Science, Marya Lieberman, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

In January of 2017 children at a state run hospital in Veracruz, Mexico were given fake chemotherapy drugs that contained none of the active pharmaceutical ingredient (API). Multiple cases from various countries involving falsified chemotherapy drugs have been reported, however no statistics are available for the frequency of falsification of these drugs. Low and Middle income countries often do not have the resources and instrumentation available to easily test medications. I developed a paper analytical device(chemoPAD) to detect the API of four commonly used chemotherapy drugs : methotrexate, doxorubicin, cisplatin and oxaliplatin. The quality of these drugs is challenging to assess because they are provided in very low concentrations and are hazardous to handle. Color tests were developed to detect these drugs at room temperature on a paper platform using only about 65 µL of material. The paper card was engineered to minimize the exposure of the user to the drug solution. Blind validation studies were performed to see whether the test cards could detect the most common types of falsified chemotherapy formulations. The test cards were analyzed with image analysis software and compared to traditional HPLC analysis. This inexpensive device could be used at hospitals and clinics in the developing world to ensure that patients are not treated with fake chemotherapy drugs.



**Poster Presentation:**

## Deposit Type Normalized Rare Earth Element Signatures for Nuclear Forensic Applications

Tyler Spano, College of Engineering, Civil Engineering and Geological Sciences, Peter Burns, Chemistry and Biochemistry and Civil Engineering and Geological Sciences, Corinne Dorais, College of Engineering, Grace Carpenter, Devonee Freet, Enrica Balboni, Thomas Wheeler, Environmental Engineering, Antonio Simonetti, University of Notre Dame, College of Engineering, Dept. of Civil Engineering and Geological Sciences

Provenance determination for uranium-rich materials is a critical objective of nuclear forensic analysis. Rare earth element (REE) distributions within uranium ores have seen extensive use as forensic indicators, but quantifying and correlating trace element signatures for U ores to known deposits has thus far involved intricate statistical analyses. Average chondrite normalized (CN)-REE signatures for important U deposit types (DT) worldwide have been calculated and employed to evaluate U ore paragenesis using a simple linear regression analysis. Average DT-CN-REE signatures for unconformity-related, vein type, sandstone, intrusive, and metamorphic type U deposits were established. Uranium ores and derivative materials (uranium ore concentrate) of known origins were treated as unknowns, and in all cases the deposit type from which the sample originated could be positively identified using this method. This novel technique provides a means for rapid assessment of the deposit type of U ores based on their REE abundances.

**Poster Presentation:**

## Loss of APC Mediates Doxorubicin Chemoresistance in Breast Cancer

Casey Stefanski[1,2], Kaitlyn Keffler[1.2], and Jenifer R. Prosperi[1-3]
[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

Chemoresistance is one of the leading causes of breast cancer related deaths. Understanding the molecular basis for chemoresistance is essential for the advancement of novel therapeutic approaches to ultimately improve patient outcomes. The *Adenomatous Polyposis Coli* (*APC*) tumor suppressor is either mutated or hypermethylated in up to 70% of sporadic breast cancer; however, little is known about how loss of APC contributes to chemoresistance. Using the $Apc^{Min/+}$ mouse crossed to the Polyoma middle T antigen (PyMT) transgenic model, we have shown that APC loss decreased cisplatin and doxorubicin-induced apoptosis. Herein, we investigate APC-induced molecular changes that promote resistance to doxorubicin. Ongoing studies have shown that MMTV-PyMT;$Apc^{Min/+}$ cells exhibited increased activity of glutathione S transferase (GST), which aids in drug detoxification. In addition, preliminary studies have also shown decreased γH2AX in MMTV-PyMT;$Apc^{Min/+}$ cells treated with doxorubicin. Having previously shown that MMTV-PyMT;$Apc^{Min/+}$ cells have an increased tumor initiating cell (TIC) population and multidrug resistance protein 1 (MDR1) expression, next we investigated MDR1 inhibition on restoring doxorubicin-mediated apoptosis in MMTV-PyMT;$Apc^{Min/+}$ cells. APC loss increased MDR1 activity as measured by reduced intracellular fluorescent calcein, which was restored to WT control levels by the MDR1 inhibitor, PSC833. We also examined if MDR1 inhibition in MMTV-PyMT;$Apc^{Min/+}$ cells could restore doxorubicin-mediated apoptosis. In addition, MDR1 inhibition in MMTV-PyMT;$Apc^{Min/+}$ cells reduced TIC population but not to the level of WT Control. Future studies will investigate whether loss of APC alters doxorubicin-induced phosphorylation of ATM and ATR and whether MDR1 inhibitor can restore doxorubicin-induced γH2AX expression in MMTV-PyMT;$Apc^{Min/+}$ cells. Taken together, targeted combination therapy with chemotherapy could be beneficial to overcome chemoresistance.

**Poster Presentation:**

## Lunar Sample 60025: A Story of Multiple Lithologies

Michael Torcivia, College of Engineering, Clive Neal, University of Notre Dame, College of Engineering, Dept. of Civil Engineering and Geological Sciences

The Moon is thought to have formed from a giant impact between the proto-Earth and a Mars-sized planetesimal named Theia. The debris from this collision then quickly coalesced to form the Moon. After accretion, the Moon then underwent a period of differentiation best explained by the lunar magma ocean (LMO) model, where the upper ~500 km or all of the Moon experienced melting and then subsequently cooled and differentiated. Apollo 16 lunar sample 60025 is thought to be a product of the LMO and one of the earliest examples we have of the primordial lunar crust, derived from the LMO. As a member of the ferroan anorthosite suite (FANs), 60025 has proved to be a challenge for geochronologists to precisely date in large part due to its low concentrations of relevant radiogenic isotopes. Despite this challenge, two separate studies have successfully yielded two distinct age dates for 60025 using the same Sm-Nd isotopic system (4.44±0.02 Ga and 4.367±0.011 Ga). These ages – while similar – are not within error of one another, so this raises the question as to how a single rock can yield two distinct crystallization ages. Using a mixture of petrographic, electron microprobe (EMP), and laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) analyses of five 60025 thin sections, this study provides valuable insight regarding the nature of this sample as a postulated flotation cumulate of the LMO and a sample of the early lunar crust. As a result of this comprehensive major, minor, and trace element analysis, this study offers an explanation for the discordant ages reported in the literature and the implications for future geochronologic studies of lunar crustal material. Preliminary data supports the conclusion that 60025 represents a mixed lithology of lunar material with each lithology corresponding to a different age.

**Poster Presentation:**

## Does Stringent Selection Boost or Reduce the Rate of Evolutionary Adaptation?

Yueh-Fu O. Wu[1,2], Alexander G. Madey[1], Luis Erana-Salmeron[3], and Holly V. Goodson[1,2]
[1]Department of Chemistry and Biochemistry, [2]Integrated Biomedical Sciences Graduate Program, [3]Department of Mechanical and Aerospace Engineering, University of Notre Dame

Evolution is classically thought to occur gradually. Nevertheless, the fossil record suggests that evolution occurs in sudden bursts, followed by relative stasis: a process described as "punctuated equilibrium". The goal of this study is to address the question of why the rate of evolution changes through time. A standard explanation is that evolution occurs fastest when selection is imposed and the speed of evolution is related to the intensity of the selection. However, a stringent selective pressure imposed on a population could slow down its ability to adapt by reducing the overall diversity. One of the most stringent selections a population may encounter is food limitation. Thus, we hypothesize that the overall rate of evolution would depend on the abundance of food. Our approach is to use both in vitro and in silico methods to compare the adaptation of clonal asexual organisms (yeast) in two different continuous culture environments: a turbidostat (culture is fed when it reaches a certain turbidity, representing unlimited food) and a chemostat (culture is fed regularly, after a long period of time, representing organisms competing for limited food). To measure the adaptation of the organism, a non-nutrient stress will be applied to both culture systems. We predict that organisms will adapt to a non-nutrient stress faster in the turbidostat than the chemostat. So far, our preliminary data suggests that in the same amount of elapsed time, the rate of evolution is faster in the turbidostat and supports our hypothesis that the overall rate of evolution would increase without stringent selection.

**Poster Presentation:**

## Modeling the Dynamics of Cdc42 Oscillation in Fission Yeast

Bin Xu, Alexandra Jilkine, University of Notre Dame, College of Science, Dept. of Applied and Computational Mathematics and Statistics

Regulation of polarised cell growth is essential for many cellular processes, including spatial coordination of cell morphology changes during growth and division. We present a mathematical model of the core mechanism responsible for the regulation of polarised growth dynamics during the fission yeast cell cycle. We focus on the dynamics of a small GTPase Cdc42, which directs the polarised growth in fission yeast. The model is based on the competition of growth zones of Cdc42 localised at the cell tips for a common substrate (inactive Cdc42) that diffuses in the cytosol. We consider several potential ways of implementing negative feedback between Cd42 and its GEF in this model that would be consistent with the observed oscillations of Cdc42 in fission yeast. We analyse the bifurcations in this model as the cell length increases, and total amount of Cdc42 and GEF increase. We find that a stable oscillation and a stable steady state can coexist, which is consistent with the experimental finding that only 50% of bipolar cells oscillate. The mean amplitude and period can be tuned by parameters involved in the negative feedback. We link modifications in the parameters of the model to observed mutant phenotypes. Our model suggests that negative feedback is more likely to be acting through inhibition of GEF association rather than upregulation of GEF dissociation.

**Poster Presentation:**

## Reprogramming Leukemic Cells Reveals Potential for Disease Modeling and Therapeutic Development

Amanda Yamasaki, College of Science, Biological Sciences, Nicholas E. King, Biological Sciences, Athanasia Panopoulos, University of Notre Dame, College of Science, Dept. of Biological Sciences

Acute myeloid leukemia (AML) is the most common form of acute leukemia affecting adults, characterized by defects in hematopoietic differentiation that lead to accumulation of immature myeloid cells in patients. Although AML is a complex disease that can present with a variety of genomic aberrations affecting prognosis, standard course of therapy is virtually identical for all cases – cytotoxic chemotherapy leading to remission in 50-85% of cases, after which most patients suffer fatal relapse in less than two years. Patients in remission are candidates for hematopoietic stem cell therapy (HSCT), but autologous transplantations cannot correct for disease-causing genetic aberrations, and allogeneic transplantations are hampered by lack of matched donors and risk of severe graft-versus-host disease (GVHD). Further study of AML is required – both to gain a better understanding of how diverse disease genetics can affect development and progression of the disease, and to begin to develop more personalized and effective treatments. Reprogramming – the process of returning fully differentiated cells to an embryonic state and creating induced pluripotent stem cells (iPSCs) that can be differentiated in vitro into any number of functional cell types – provides a novel approach to study this disease. To this end, we reprogrammed hematopoietic stem cell-enriched (CD34+) cells isolated from the bone marrow of a relapsed/refractory AML patient and the AML cancer cell line HL-60. While both iPSCs generated from the primary AML sample and the HL-60 leukemic cell line display expression of pluripotent genes and cell surface markers at similar levels to iPSCs generated from disease-free cells, primary AML-derived iPSCs show no evidence of the original leukemic genetic aberrations. This supports the potential use of reprogramming as a therapeutic approach in the treatment of diseases with a genetic basis, without relying on more complicated gene editing processes, suggesting that in the future, autologous HSC transplants may become a more viable treatment option. In contrast, iPSCs generated from the HL-60 leukemic cell line retain many of the genetic and chromosomal abnormalities present in the parent population, and appear to be deficient in differentiation potential. These iPSCs provide a useful tool to study the development and progression of AML.

**Oral Presentation:**

## Loss of MTSS1 Results in Increased Metastatic Potential in Pancreatic Cancer

Ann Zeleniak, College of Science, Biological Sciences, Mary Brinkman, Weixin Huang, College of Science, Reginald Hill, University of Notre Dame, College of Science, Dept. of Biological Sciences

Pancreatic ductal adenocarcinoma (PDAC) has a 5-year survival rate of 7%. This dismal outlook is largely due to the inability to diagnose the disease before metastasis occurs. 53% of patients afflicted with pancreatic cancer are diagnosed at metastatic stage. Thus, there is a critical need to better understand what causes early tumor cell dissemination and metastatic progression in this disease. One of the hallmarks of early stages of PDAC is inflammation. While many studies have focused on elucidating the mechanisms by which inflammation drives PDAC progression, few have focused on the role inflammation plays in metastasis. Using a novel inflammation-driven mouse model of PDAC, we uncovered a subset of genes that were not only regulated by increased inflammation, but also correlated with poor PDAC patient prognosis. Here, we functionally test the role of one of the genes found in this subset involved in metastatic progression, namely, metastasis suppressor protein 1 (MTSS1). We show that loss of MTSS1 leads to increased invasion and migration in PDAC cell lines. Moreover, PDAC cells treated with cancer-associated fibroblast-conditioned media also have increased metastatic potential, which is augmented by loss of MTSS1. Also, overexpression of MTSS1 in PDAC cell lines leads to a loss of migratory potential *in vitro* and an increase in overall survival *in vivo*. Additionally, we present a novel regulatory mechanism for the stabilization of MTSS1 via the tumor suppressor protein, phosphatase and tensin homolog (PTEN). Our data show that PTEN loss results in increased metastatic potential and decreased MTSS1 expression. Furthermore, we show that ectopic MTSS1 expression rescues this effect. Additionally, we demonstrate that PTEN forms a complex with MTSS1 to stabilize it from proteasomal degradation. Finally, we show that the inflammatory tumor microenvironment, which makes up over 90% of PDAC tumor bulk, downregulates PTEN expression via miRNA-23b, potentially uncovering a novel extrinsic mechanism of MTSS1 regulation. Collectively, these data offer new insight into the role and regulation of MTSS1 in suppressing tumor cell invasion and migration and the molecular mechanisms that could be leading to early cell dissemination in PDAC.