UNIVERSITY OF NOTRE DAME

College of Science

Inaugural COS-JAM for Graduate Students & Postdoctoral Fellows

Thursday – May 4, 2017

Jordan Hall

Schedule:

Morning Session (10-12:00pm): poster session in Jordan Galleria – 44 participants total
(snacks/drinks in Galleria; posters taken down at end of day at 3:30pm)

Informal Q&A Table – Graduate Career Services, Office of Grants & Fellowships, Office for Postdoctoral Scholars

Lunch (12-1:30pm): Jordan Galleria – participants, discussants & moderators only

Panel Discussion (12:15-1:15pm): 322 Jordan – career development, CV advice, grants, etc.

"From Collegian to Colleague: Setting Yourself up for Success!"
(Graduate Career Services, Office of Grants & Fellowships, Office for Postdoctoral Scholars)

Afternoon Session (1:30-3:30pm): podium presentations in Jordan auditoriums (101 & 105) – 16 participants total
(snacks/drinks in Galleria; 2 mixed-subject concurrent sessions)

Funding for this event was provided by the College of Science. Many thanks to the following individuals for help and support: Dean Mary Galvin, Associate Dean Mike Hildreth, Crislyn D'Souza-Schorey, Brian Baker, Andrew Sommese, Chris Kolda, Jeff Diller, Rebecca Wingert, Holly Goodson, Brandon Ashfeld, Zhiliang Xu, Mark Caprio, Peter Cholak, Dom Chaloner, Sharon Stack, Allen Utterback, Lisa Mercurio, Kim Kirkpatrick, Valli Sarveswaran, Samantha Lee, Larry Westfall, Michelle Whaley, Susan Monroe, Jenna Mrozinske, Mark Olsen, Mauna Dasari, Dani Brake, Guido Felipe Camargo Espana, Chissa Rivaldi, Laura Grieneisen, Emily Amenson-Lamar, Victoria Makuru, Katie O'Reilly, Kelly Heilman, and the graduate students and postdoctoral fellows who contributed to the success of this first-ever event.

PANEL DISCUSSANTS (morning session – informal in Jordan Galleria & panel at 12:15-1:15pm – 322 Jordan)

Larry Westfall, Director Graduate Career Services at the University of Notre Dame, is a former human resources leader with over 25 years of national and international experience in talent management, employee relations, organizational change, and career development. Over the course of his career he has worked in both the public and private sector in energy, financial services, healthcare, and higher education. He received a bachelor's degree from Purdue University and pursued graduate studies at Georgia Southern University. He is a member of the Graduate Career Consortium, the MBA Career Services & Employer Alliance, the HR Management Association of Chicago, and the National Eagle Scout Association. He is certified as a Senior Professional in Human Resources, sits on the Board of Directors for the Eagle Lake Sailing Club, and is a volunteer advocate for the Hinsdale Humane Society. Larry has a record of success in helping people and organizations achieve the change they seek for future success and has a passion for career and professional development. He is a trusted advisor and coach and has helped numerous individuals over the years attain their personal and professional aspirations.

Valli Sarveswaran, Ph.D. is the Associate Program Director with the Office for Postdoctoral Scholars at the University of Notre Dame. As the Associate Program Director, Valli is responsible for mentoring postdoctoral scholars in career exploration and planning. In addition to being responsible for postdoctoral professional development, he also oversees appointment procedures and policies and foster a strong and interactive postdoctoral community.

He was previously, the Program Director of McNair Scholars Program at Cleveland State University, Cleveland OH for more than eight years. The McNair Scholars Program is a federally funded program that prepares undergraduate students for graduate schools. Valli has held postdoctoral research positions at the Universities of Notre Dame, Kentucky, and Winnipeg over five years. He has been on academic administrative roles for more than thirteen years.

He holds a BS in Chemistry from the University of Jaffna, Sri Lanka and a PhD in Organometallic Chemistry from the University of Cambridge, England.

PANEL DISCUSSANTS (cont.)

Samantha Y. Lee, Ph.D. is the Program Director of the Graduate School's Office of Grants and Fellowships at the University of Notre Dame. As the Program Director, Samantha is responsible for the overall management of the office, providing leadership and expertise in grantsmanship, managing several prestigious fellowship competitions, and ensuring that services provided by the office reflect the priorities of Notre Dame graduate students.

Samantha has over six years of experience in fellowship advising as an applicant and advisor at Rutgers, The State University of New Jersey. She has helped numerous undergraduate and graduate students generate successful merit-based grant and fellowship applications. Samantha has extensive experience in both advising students across disciplines and designing in-person and online grant writing and training curriculum. She has won numerous competitive fellowships and grants including the U.S. Department of Agriculture - National Institute of Food and Agriculture Postdoctoral Fellowship, the Northeast Sustainable Agriculture Research and Education Grant, the National Science Foundation Graduate Research Fellowship, and many others. In addition, she has won several graduate research awards such as the Excellence in Graduate Studies by the Theobald Smith Society and the Mycological Society of America's Graduate Fellowship. She has held numerous leadership and service positions at Rutgers and professional societies including the American Association of University Women, the American Phytopathological Society, and the Mycological Society of America.

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

Garima Agrahari: *Streptococcus pyogenes* Employs Multiple Mechanisms of C3b Inactivation to Inhibit Phagocytosis

Marwa Asem: The Role of Wnt5a Signaling Pathway in Ovarian Cancer Progression

Julia Beck: Role of EACA on Plasminogen Binding and Activation by Streptokinase

Pavel Brodskiy: The Mechanical Regulation of Mitotic Rounding in Epithelia

Guido Felipe Camargo Espana: Simulating Chikungunya Outbreaks in Colombia with an Agent-Based Model

Katelyn Carothers: Identification of a Host Keratinocyte Cell Target of *Streptococcus pyogenes* Toxin Streptolysin S

Brooke Chambers: tfap2a is a Novel Regulator of Renal Progenitor Fate during Kidney Development

Joseph Chambers: Chemical Genetic Screen Reveals Novel Role for PPAR Signaling in Renal Progenitor Development

Alexandra Chirakos: Investigating the Molecular Role of Esx-1-Substrates in Protein Transport

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

Mauna Dasari: Understanding Change: Gut Microbial Community Dynamics Over Time

David Dik: Muropeptide Binding and the X-Ray Structure of the Effector Domain of the Transcriptional Regulator AmpR of *Pseudomonas aeruginosa*

Bridgette Drummond: Modeling Podocyte Diseases and Development with Zebrafish

Micah Ferrell: Differential N-Terminal Acetylation of S18 Paralogs by *Mycobacterium marinum* RimI

Francisco Fields: Discovery and Rational Design of Linear Antimicrobial Peptides from a Circular Bacteriocin

Mark Fraser: Effectiveness of Sub-Therapeutic Staurosporine on Inhibition of Budding and Replication of Lipid-Enveloped Viruses

Stefan Freed: High-Throughput Multiparametric Scoring of Misfolding Defects in Non-Ketotic Hyperglycinemia

Orlando Gomez: Commissioning of the High Efficiency Total Absorption Spectrometer (HECTOR)

Ian Guldner: An Integrative Platform for Three-dimensional Quantitative Analysis of Spatially Heterogeneous Metastasis Landscapes

Matthew Hall: A Measurement of the Nuclear Levels in 19Ne using GODDESS

Karlyn Harrod: Infectious Systems of Uncertainty: The Effect of Partial Observation on Inferences of Epidemiological Parameters

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

Jamison Jangula: Mechanical Repair of Micro-Lesions in Epithelial Tissues

Ju-Young Kim: Surface Plasmon Resonance (SPR) and Surface Enhanced Raman Scattering (SERS) Combinded Spectroscopy for Elucidating Protein-Ligand Recognition

Tyson Lager: Cell Surface Expression of the ER-Chaperone Protein GRP78 Regulates Stem Cell and Breast Cancer Cell Migration

Janice Love: The Iroquois Transcription Factor, irx1b, is Required for Proximal Tubule Development in the Zebrafish Kidney

Daniel Marous & Mark Horsman: Whole-Genome Sequencing and Analysis of Two Burkholderiaceae Members of the Secondary Metabolite-Producing Betaproteobacteria

Amanda Marra: Genetic Mechanisms of Multiciliated Cell Development during Renal Ontogeny

Rachel Miller: Development of Synthetic Biological Tools for Analytical Applications in Technology Limited Settings

Elvin Morales: emx1 is Essential for Distal Segment Development in the Zebrafish Pronephros

Darby Nelson: Using Stark Shifts to Understand the Driving Forces in Plasmonic Catalysis

Anh Nguyen: Quantitative Online Sheath-Flow Surface Enhanced Raman Detection for Liquid Chromatography

Trung Nguyen: Matrix Metalloproteinase-9: A Pharmacological Target to Treat Diabetic Foot Ulcers

Craig Reingold: Extracting Statistical Properties of Samarium Isotopes Using the Oslo Method

Felicia Roland: Dye-Loaded Core-Shell Au-SiO2 Nanoparticles for Cancer Theranostics

Emily Shangle: Combination of Capillary Electrophoresis and Sheath Flow SERS for Metabolite Detection in Biological Fluids

Samantha Sherman: Exceptional Stewart-Gough Platforms and Segre Embeddings

Enrico Speri: Synthesis and Biological Studies of the Cinnamonitrile Class of Molecules as Antibiotic Potentiators for Methicillin-Resistant *Staphylococcus aureus* (MRSA)

Subha Subha: Exploring the Aging of MoS¬2 through Ambient Pressure X-ray Photoelectron Spectroscopy

Chien-Wei Wang: Multiple Pathways Activate Cip1 to Inhibit Cd 1 k1-G1 Cyclins upon Stress

Justin Wilcox: Unprecedented Eukaryotic Gut Microbiome Diversity is Governed by Conserved Ecological Processes in a Non-Human Primate

Qinfeng Wu: Intercellular Calcium Waves are Controlled by Morphogen Signaling during Organ Development

Amanda Yamasaki: Generation of Induced Pluripotent Stem Cells from Acute Myeloid Leukemia

Ann Zeleniak: Loss of MTSS1 Results in Increased Metastatic Potential in Pancreatic Cancer

AFTERNOON PODIUM SESSION (1:30-3:30pm – 101 & 105 Jordan)

Jordan 101 (moderator: Dani Brake)

1:30 – Amanda Yamasaki: Generation of Induced Pluripotent Stem Cells from Acute Myeloid Leukemia

1:45 – Dharsan Soundarrajan: Ca2+ Dynamics in Epithelial Networks

2:00 – Rachel Oidtman: Disentangling the Relative Roles of Importation and Weather in Driving Interannual Variation in Dengue Epidemics in Guangzhou, China

2:15 – Trung Nguyen: Matrix Metalloproteinase-9: A Pharmacological Target to Treat Diabetic Foot Ulcers

2:30 – Kelsey DiPietro: Numerical Methods for Modeling Electrostatic Deflections

2:45 – Francesco Pancaldi: Micro-scale Computational Model of Fibrin Networks Mechanics

3:00 – Susan Coiner-Collier: Cross-sectional Geometry of the Mandibular Corpus and Food Mechanical Properties in Extant Primates

3:15 – Megan Levis: Mechanotransduction in Epithelial Wound Healing

Jordan 105 (moderator: Guido Felipe Camargo Espana)

1:30 – Amir Siraj: Estimating the Population at Risk of Zika in the Asian Region

1:45 – Anthony Rosales: Development and Application of the Q2MM Method to Metal and Enzyme Catalyzed Reactions

2:00 – Margaret Regan: Homotopies for Overdetermined Systems with Applications in Computer Vision

2:15 – Evercita Eugenio: An Adaptive Mechanism for Multiple Queries in Differentially Private Data Synthesis

2:30 – Nur Mustafaoglu: Purification of Antibodies by Small Molecule-Based Affinity Chromatography via Nucleotide Binding Site

2:45 – Alyssa Lesko: Adenomatous Polyposis Coli Regulates Cell Motility through C-Terminal Interactions with the Cytoskeleton

3:00 – Claire Bowen: Statistical Allocation for Epsilon (SAFE) and Its Application in Differentially Private Release and Analysis of Voter Registration Data

3:15 – Gary Beane: Surface Plasmon Polariton Interference in Gold Nano-Plates

ABSTRACTS

(alphabetical by presenter)

Streptococcus pyogenes Employs Multiple Mechanisms of C3b Inactivation to Inhibit Phagocytosis

Garima Agrahari, College of Science, Kristofor Glinton, College of Science, Victoria Ploplis, Chemistry and Biochemistry, Shaun Lee, Biological Sciences, Zhong Liang, Chemistry and Biochemistry, Francis Castellino, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

Group A *Streptococcus pyogenes* (GAS) is a spherical, Gram-positive bacterium that is responsible for numerous diseases with diverse clinical manifestations, specifically in humans. GAS can cause common illnesses such as impetigo, pharyngitis, and scarlet fever but can also cause life-threatening sequelae, such as necrotizing fasciitis, streptococcal toxic shock syndrome (STSS), and acute post-streptococcal glomerulonephritis. GAS infections remain a leading cause of global mortality and morbidity. Approximately 18 million prevalent cases are found to be severe with nearly 2 million new cases reported per year worldwide. Although GAS remains uniformly susceptible to penicillin, methods for the prevention of GAS associated diseases are inadequate. Therefore, a better understanding of the cellular and molecular mechanisms of GAS infection would facilitate in designing and developing broad-spectrum drugs and diagnostic tools. To establish infection, GAS must develop evolutionary strategies to evade the host innate immune system, especially complement-mediated elimination of the microbe. In general, GAS inhibits the amplification of the complement cascade on its cell surface by facilitating the degradation of C3b, an opsonin, to an inactive product, iC3b, catalyzed by Factor I (FI) and its cofactor, Factor H (FH), with or without participation of human host plasmin (hPm). GAS recruits FH to its cell surface via FH receptors, which are transcriptionally controlled by the two-component CovRS system. The manner in which FI/FH and hPm function together on GAS cells is unknown. Using the GAS strain AP53, which binds host human plasminogen (hPg)/hPm directly via a hPg/hPm surface receptor, Plasminogen binding Group A Streptococcal M-like protein (PAM), we have shown that both FI/FH and hPm sequentially cleave C3b. While FI/FH proteolytically cleaves C3b into iC3b, hPm cleaves iC3b into multiple smaller peptides. These results suggest that GAS utilizes diverse mechanisms to degrade C3b and thus protects bacterial cells from the host complement response.

The Role of Wnt5a Signaling Pathway in Ovarian Cancer Progression

Marwa Asem[1, 2, 3], Allison Young[3], Carlysa Oyama[3], Rebecca Burkhalter[3], Steven Buechler[4], Daniel L. Miller[5] and M. Sharon Stack[1, 2, 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, University of Notre Dame, Notre Dame, IN, [5]Department of Pathology, The 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.

Surface Plasmon Polariton Interference in Gold Nano-Plates

Gary Beane, Chemistry and Biochemistry, Paul Johns, Chemistry and Biochemistry, Tuphan Devkota, College of Science, Kuai Yu, Science and Technology, Gregory Hartland, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

Transient absorption and Fourier imaging techniques were used to study the optical properties of gold nano-plates. We observe that for sufficiently thin gold nano-plates, transient absorption microscopy (TAM) images show an oscillatory variation in absorbance across the length of the plate. We demonstrate, using COMSOL simulations, that this pattern results from the interference between the wave-vectors of the surface plasmon polaritons (SPPs) at either the glass-gold ('bound mode') or the gold/dielectric interface ('leaky mode'). Through changing the dielectric material above the gold nano-plate from air to water, we observe a change in the spatial period of the interference pattern from 1.25 to 4.0 μm at 720 nm. In conjunction with the wave-vector of the leaky mode obtained from Back Focal Plane (BFP) imaging, we are able to directly extract the wave-vector of the bound mode. This is found to be in good agreement with the COMSOL simulations.

Role of EACA on Plasminogen Binding and Activation by Streptokinase

Julia Beck, College of Science, Victoria Ploplis, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry, Francis Castellino, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

Plasminogen (Pg) conversion to the serine protease plasmin via host and exogenous factors results in activation of the human fibrinolytic system and ultimately degradation of fibrin and extracellular matrices. The two host activators of plasminogen, tissue plasminogen activator (tPA) and urokinase plasminogen activator (uPA), proteolytically cleave the Arg560-Val561-hPg bond. Our lab has previously performed extensive studies on the effect of Cl- ions and EACA on the activation of plasminogen via uPA and found that NaCl and EACA have opposite effects on plasminogen activation. Plasminogen activation is stimulated in the presence of EACA and inhibited in the presence of NaCl. This is due to the ability of plasminogen to adopt an either open or closed conformation. In the presence of Cl- ions, plasminogen maintains the closed, activation resistant conformation. Within plasminogen there are two Cl- ion binding sites each within the LBS of kringles 2 and 4, which stabilize intramolecular interactions between the serine protease domain and activation peptide, respectively. This conformation can be shifted to open in the presence of EACA. Part of the N-termini of plasminogen can be cleaved resulting in Lys78-hPg, which maintains the open conformation. The virulence factor streptokinase (SK) that is secreted by Group A Streptococcus (GAS), a bacterial pathogen responsible for diseases including rheumatic heart disease, impetigo, and necrotizing fasciitis, activates Pg through a unique indirect proteolytic mechanism. SK forms a complex with plasminogen which then activates free plasminogen. The role of EACA on activation of both Glu1-hPg and Lys78-hPg via SK is not well understood. Preliminary results indicate that EACA inhibits SK from binding to plasminogen resulting in a loss of plasminogen activation. Establishing the function of EACA in SK-mediated activation of plasminogen could lead to potential therapeutic advances. These studies examined the role of EACA in plasminogen binding and activation by SK.

Statistical Allocation for Epsilon (SAFE) and Its Application in Differentially Private Release and Analysis of Voter Registration Data

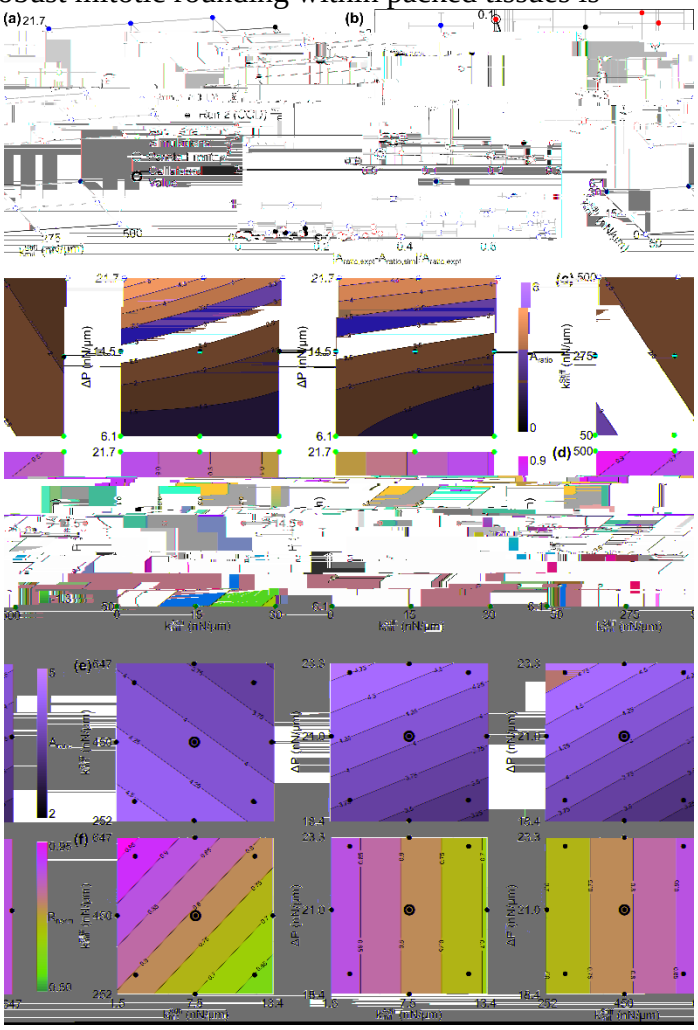
Claire Bowen, College of Science, Applied and Computational Mathematics and Statistics
Fang Liu, Applied and Computational Mathematics and Statistics, University of Notre Dame

Voter registration data is important in political science research and applications such as youth voter turnout and predicting the presidential election outcome. Voter registration data often contains sensitive information about the individuals in the data sets. One way of mitigating the privacy concern is removing identifiers in the released data. However, a data intruder can still expose personal information of the participants in the "anonymized" data by linking it to other public data sets such as healthcare data or the Personal Genome Project Data. DIfferentially Private Data Synthesis (DIPS) techniques produce synthetic data or pseudo individual records at a preset level of privacy protection. Although DIPS provides a strong and robust privacy guarantee, statistical inferences drawn from the synthetic data can be poor due to the large amount of noise added to the data. We propose and apply a new approach called Statistical Allocation for Epsilon (SAFE) on voter registration data that allocates the privacy budget based on the statistical significance of the data's parameters. From the simulation study, SAFE outperforms DIPS alone by significantly improving the statistical inferences conducted on the voter registration data.

The Mechanical Regulation of Mitotic Rounding in Epithelia

Pavel Brodskiy, College of Engineering, Zhiliang Xu, Mathematics, Cody Narciso, College of Engineering, Chemical Engineering, Aboutaleb Amiri, College of Science, Ali Nematbakhsh Wenzhao Study, Jeremiah Zartman, University of Notre Dame, College of Engineering, Dept. of Chemical and Biomolecular Engineering and Mark Alber, University of Notre Dame, College of Science, Dept. of Applied and Computational Mathematics and Statistics
a Department of Applied and Computational Mathematics and Statistics, University of Notre Dame, Notre Dame, IN 46556, USA b Department of Chemical and Biomolecular Engineering, University of Notre Dame, Notre Dame, IN 46556, USA c Department of Physics, University of Notre Dame, Notre Dame, IN 46556, USA d Department of Mathematics, University of California, Riverside, CA 92521, USA

Mitotic rounding during cell division is critical for preventing daughter cells from inheriting an abnormal number of chromosomes, a condition that occurs frequently in cancer cells. Cells must significantly expand their apical area and transition from a polygonal to circular apical shape to achieve robust mitotic rounding in epithelial tissues, which is where most cancers initiate. However, how cells mechanically regulate robust mitotic rounding within packed tissues is unknown. Here, we analyze mitotic rounding using a newly developed multi-scale sub-cellular element computational model that is calibrated using experimental data. Novel biologically relevant features of the model include separate representations of the sub-cellular components including the apical membrane and cytoplasm of the cell as well as a detailed description of cell-cell interactions at the tissue scale. Regression analysis of predictive model simulation results reveals the relative contributions of osmotic pressure, cell-cell adhesion and cortical stiffness to mitotic rounding. Mitotic area expansion is largely driven by regulation of cytoplasmic pressure. Surprisingly, mitotic shape roundness within physiological ranges is most sensitive to variation in cell-cell adhesivity and stiffness. An understanding of how perturbed mechanical properties impact mitotic rounding has important potential implications on, among others, how tumors progressively become more genetically unstable due to increased chromosomal aneuploidy and more aggressive.



Simulating Chikungunya Outbreaks in Colombia with an Agent-Based Model

Guido Felipe Camargo Espana, Biological Sciences, John Grefenstette, Graduate School of Public Health, University of Pittsburgh, Hernando Diaz, Electrical and Electronics Engineering School, National University of Colombia, Fernando delahoz-Restrepo, School of Public Health, National University of Colombia, Donald Burke, Graduate School of Public Health, University of Pittsburgh, Willem van Panhuis, Graduate School of Public Health, University of Pittsburgh, Alex Perkins, University of Notre Dame, College of Science, Dept. of Biological Sciences

It is crucial to optimally distribute resources to halt the spread of vector-borne diseases to new regions. Between 2013 and 2016, almost two million chikungunya cases were reported, as the first chikungunya outbreak took place in the Americas. Colombia, one of the most affected countries by the epidemic, reported around half a million cases. Due to the unavailability of a vaccine, governments focused on vector control programs to reduce the impact of the epidemic. However, the regional benefit of these interventions remains unknown. We quantified the effect of vector control programs in different regions with an agent-based model of chikungunya transmission calibrated to Colombia. We fit our model to represent individual and population-level characteristics of 45 million people in terms of geography, climate and demography. We calibrated the transmission model parameters and the specific vector control parameters to incidence reports of the first 24 weeks of the outbreak. Then, we simulated the epidemic at a national level under various vector control scenarios and contrasted their attack rates to a scenario without vector control. Our simulations showed different reduction rates among regions when vector control was incorporated. The reduction rates cause by vector control were higher for the Amazonian (72%), Pacific (64%), Orinoquía (64%), and Andean (63%) regions, than for the Insular (45%) and Caribbean (44%) regions. We validated our simulations with the latest reports available by region (2014-2016). Overall, the model predicted the shape and magnitude of the incidence curves reported in five out of six regions of Colombia. The reports of the Andean, Caribbean, Pacific, and Amazonian regions closely matched scenarios with high level of vector control, while the epidemic curve of the Orinoquía region suggested low levels of vector control. Our results highlight the importance of computational models to assess the impact of intervention programs and to potentially predict the magnitude of similar outbreaks. Our model could be used as a tool to optimally distribute resources for vector control campaigns in future epidemics. Finally, we believe that this platform can be used to model similar transmitted viruses such as zika or dengue.

Identification of a Host Keratinocyte Cell Target of *Streptococcus pyogenes* Toxin Streptolysin S

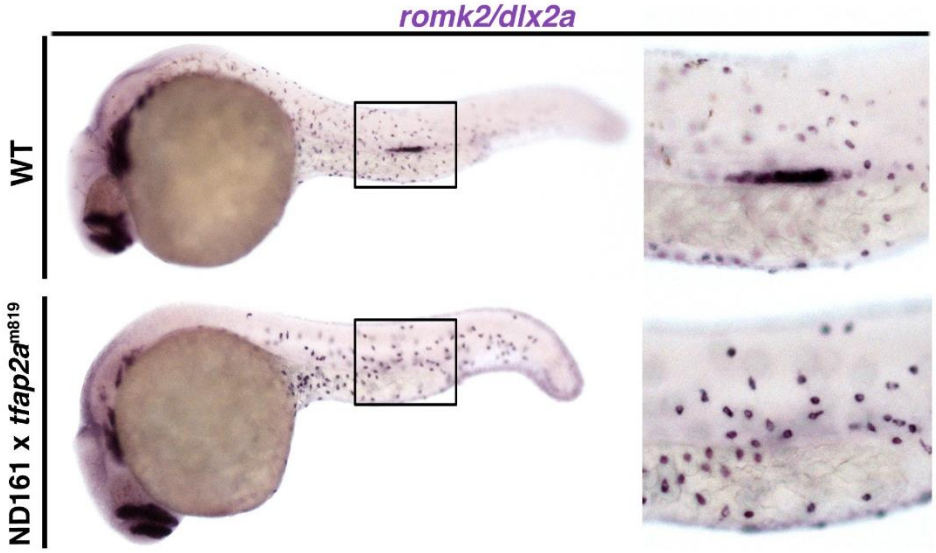
Katelyn E. Carothers[1], Rebecca A. Flaherty[1], Shaun W. Lee[1]
[1]Department of Biological Sciences, University of Notre Dame

Streptococcus pyogenes, also known as Group A Strep (GAS) is a common colonizer of human skin and mucosal surfaces, and the causative agent of diseases ranging from mild skin and throat infections to severe invasive disease and post-infection autoimmune complications. One of the most potent virulence factors produced by GAS is Streptolysin S, or SLS. SLS is a small peptide encoded by the Streptolysin-associated gene (Sag) cluster, which includes genes for the pro-toxin as well as modification and transport proteins. While the structure of SLS has not been fully elucidated, it is known to have cytolytic activity in a number of host cells, and produces a characteristic β-hemolytic phenotype in erythrocytes. Our lab has investigated the mechanisms by which SLS targets host cells and induces downstream cell signaling resulting in inflammatory responses and cell death. It has been previously demonstrated in our lab that SLS induces lysis in erythrocytes by osmotic imbalance via disruption of the ion channel Band 3. SLS is also known to have cytotoxic activity in keratinocytes that do not express Band 3, and this cytotoxicity can be reduced using the ion channel inhibitor DIDS. We therefore hypothesize that SLS targets an ion channel in keratinocytes and propose a strategy to identify this target using a biotin-tagged form of the ion channel inhibitor DIDS and a pulldown using biotin's high affinity for streptavidin-coated beads. Our data thus far demonstrates chemical modification of the sulfonic acid groups of DIDS does not affect its efficacy as an inhibitor, and that it is amenable to biotinylation. Identification of this keratinocyte target furthers our understanding of GAS pathogenesis during skin infection and how the bacteria may breach the epithelial barrier to cause more invasive disease.

tfap2a is a Novel Regulator of Renal Progenitor Fate during Kidney Development

Brooke Chambers, College of Science, Biological Sciences, Ignaty Leshchiner, Harvard University, Wolfram Goessling, Harvard University, Rebecca Wingert, University of Notre Dame, College of Science, Dept. of Biological Sciences

Occurring in 1 in 500 births, Congenital Anomalies of the Kidney and Urinary Tract (CAKUT) are the primary cause of pediatric end-stage renal disease. The central etiology of these conditions involves aberrant development of nephrons, which are the functional units of the kidney. To date, the molecular coordination of epithelial cell-fate decisions during vertebrate nephron segmentation remains poorly understood. The embryonic zebrafish pronephros has emerged as a powerful genetic system to study kidney development. At 24 hours post fertilization, the pronephros is fully formed and exhibits simple organization consisting of two parallel nephrons making cellular alterations easy to detect. Here, through a forward ENU screen, we isolated a nephron mutant with abrogated distal tubules. Whole genome sequencing revealed a lesion that disrupts splicing of transcription factor AP-2 alpha (tfap2a), thereby truncating essential transcriptional activation and DNA binding domains. Until now, tfap2a has been known as essential for neural crest and epidermis differentiation but was not appreciated to act during renal ontogeny. We found that tfap2a was dynamically expressed in zebrafish renal progenitors, eventually restricting to the distal tubules. Interestingly, during mouse embryogenesis, tfap2a expression is abundant within the developing urogenital tract encompassing structures such as the ureteric tip and distal tubules. Human tfap2a mutations result in branchio-oculo-facial syndrome (BOFS), which primarily affects craniofacial tissue, though case reports have linked tfap2a lesions to multicystic dysplastic kidney. Complementation tests between our mutant line and tfap2am819, which encodes a nonsense allele, as well as knockdown studies similarly abolished the distal tubule. Conversely, overexpression of tfap2a caused a striking expansion of distal cells. Further, tfap2a-deficiency causes perturbations in other nephron cell types such as multiciliated cells and the corpuscle of Stannius. Through a subsequent suite of functional studies, we have determined that tfap2a acts upstream of several key lineage factors necessary for nephron formation, like irx1a, tbx2b, and etv5a. Taken together, our studies have revealed novel mechanisms by which tfap2a directs cell fate during nephrogenesis. Examining the molecular activities of this conserved transcription factor in renal progenitors will shed light on the regulatory role of the mammalian homologue, AP-2α, in congenital diseases.



Chemical Genetic Screen Reveals Novel Role for PPAR Signaling in Renal Progenitor Development

Joseph Chambers, College of Science, Biological Sciences, Shahram Poureetezadi, College of Science, Rebecca Wingert, University of Notre Dame, Dept. of Biological Sciences

The genetic and molecular mechanisms directing nephron segmentation during kidney development are not well understood. Deregulation of genes involved in kidney development result in a variety of diseases broadly categorized as Congenital Anomalies of the Kidney and Urinary Tract (CAKUT). Embryonic zebrafish have a simplified kidney, the pronephros, comprised of proximal and distal segments that display conservation with mammalian nephrons, including humans, thus enabling CAKUT modeling. Through a novel chemical genetic screen, we discovered that peroxisome proliferator-activated receptor (PPAR) signaling is essential for normal nephron segment development. PPARs are a group of nuclear receptor proteins that are activated by ligands such as fatty acids and act as transcription factors by heterodimerization with retinoid X receptor (RXR) to regulate cell differentiation and perform diverse roles in metabolism. We found that treatment with the PPAR agonist bezafibrate during nephrogensis alters the balance of proximal and distal cells. Interestingly, the co-activator, *ppargc1a* mutant zebrafish, where a lesion in exon 8 with a T→A substitution results in a premature STOP codon and a loss of the RNA processing domain. ppargc1a$_{sa13186}$ development renal cysts, a hallmark of dysplastic CAKUT. Assessment of essential nephron regulators revealed that _ppargc1a _acts to inhibit _irx3b _and promote *tbx2b*. Taken together, our studies suggest a novel mechanism by which PPAR signaling coordinates lineage choices during nephrogenesis. These findings may lead to a better understanding of the therapeutic value of PPARs in relation to renal birth defects and cystic disease conditions as well.

Investigating the Molecular Role of Esx-1-Substrates in Protein Transport

Alexandra Chirakos*[1] and Patricia A. Champion[1]
[1]Department of Biological Sciences, University of Notre Dame, Notre Dame, IN 46556

Mycobacterium marinum, an opportunistic human pathogen, is an established model organism used to study the virulence of *Mycobacterium tuberculosis* (*Mtb*), the causative agent of tuberculosis (TB). A main virulence determinant of *Mtb* is the ESX-1 secretion system, which is conserved in both pathogenic and nonpathogenic mycobacterial species. Esx-1 functions to transport virulence factors across the mycobacterial cytoplasmic membrane. Generally, disruption or deletion of its core components or secreted factors leads to attenuation. Here we focus on the role of two paralogous secreted factors EspF and EspC in *M. marinum.* The genes encoding EspF and EspC are present exclusively in mycobacterial pathogens. In *Mtb*, *espF* and *espC* are required for secretion and virulence. Surprisingly in *M. marinum*, we observed differential requirements for export and virulence when compared to *M. tb*. Our study aims at elucidating the role of EspF and EspC in the *M. marinum* ESX-1 system, and to further our understanding of the variations in function of the secreted factors of the mycobacterial ESX-1 systems.

Cross-sectional Geometry of the Mandibular Corpus and Food Mechanical Properties in Extant Primates

Susan Coiner-Collier, Biological Sciences, Adam Pasquinelly, College of Science, Matthew J. Ravosa, University of Notre Dame, College of Science, Dept. of Biological Sciences

The mandibular corpus must withstand the bending, shear, and twisting forces generated by feeding. Experimental studies show relationships between dietary consistency and corpus development, such that animals raised on more mechanically challenging diets tend to have more robust mandibles with thicker cortical bone. To examine this potential functional link, we used data on dietary food mechanical properties (FMPs) to evaluate whether primates with tougher or more resistant diets demonstrate morphological signals in the mandibular corpus related to load resistance.

To test the relationship between cross-sectional corpus geometry and FMPs, we used a sample of 29 adult mandibles from 16 primate species, including both strepsirrhines and haplorhines. Each mandible was imaged using either HRXCT or microCT. Slices were extracted from the corpus at the left mandibular M1 and M2, and analyzed with BoneJ. For each slice, we calculated cortical bone area, total subperiosteal area, second moments of area along the major and minor and anatomical axes, and Bredt's formula.

Statistical analysis was performed using phylogenetic generalized least-squares multiple regressions of FMPs against geometric variables and mandible length (to control for differences in body size). Our results showed few relationships between FMPs and corpus variables. However, median toughness was positively related to Iyy/Ixx ($p = 0.008$, $R2 = 0.43$) and Imax/Imin ($p = 0.037$, $R2 = 0.29$) for M1. This result suggests that adaptations for bending resistance may be associated with tougher diets.

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

Henry Conner, Biological Sciences, Tyson Lager, College of Science, Biological Sciences, Ian Guldner, College of Science, 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 acquired by cancer cells has been challenging. We harnessed the power of iPSCs to identify embryonic mechanisms exploited by cancer. A screen comparing the cell surface proteome of iPSCs and breast cancer cells identified GRP78, a protein which is normally ER-restricted, but which 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. Although cell surface GRP78 (sGRP78) has emerged as an attractive chemotherapeutic target, understanding how sGRP78 is functioning in cancer has been complicated by the fact that GRP78 can function to regulate a variety of cellular responses, which can vary by cell type. Therefore, 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. These collective findings suggest that sGRP78 marks a stem-like population in breast cancer cells that has increased metastatic potential in vivo.

Understanding Change: Gut Microbial Community Dynamics Over Time

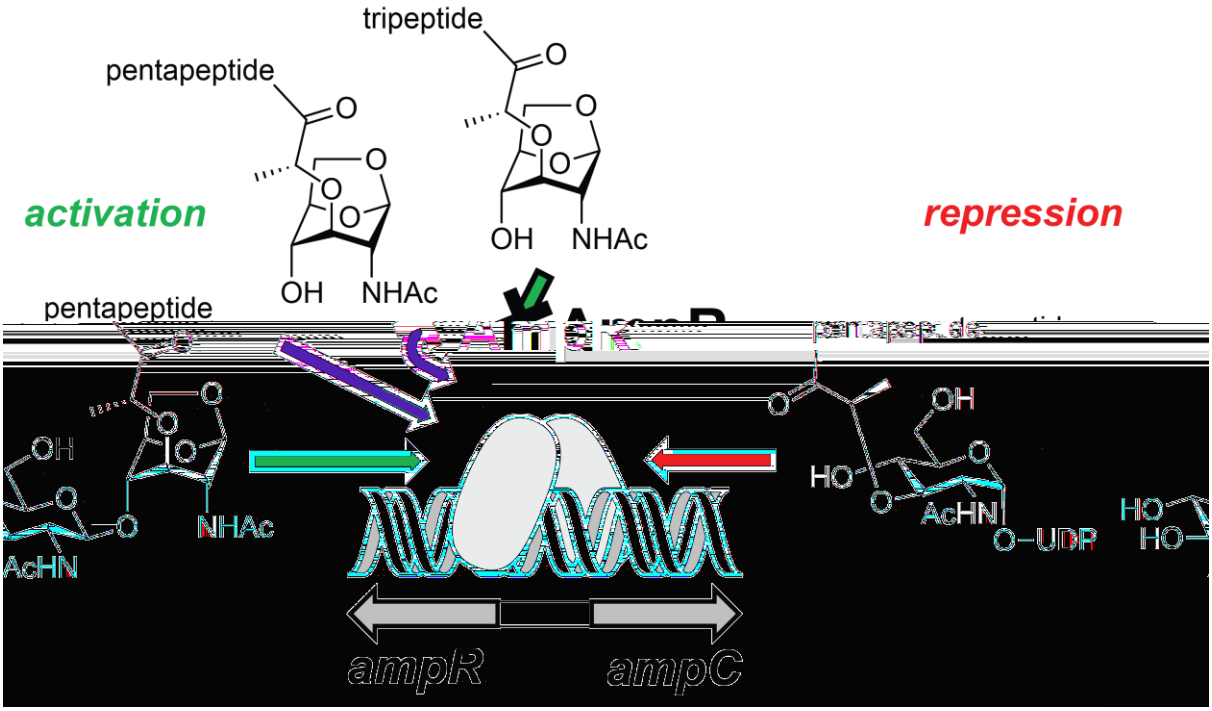
Mauna Dasari, College of Science, Biological Sciences, Ran Blekhman, University of Minnesota, Luis Barreiro, University of Montreal, Jenny Tung, Duke University, Elizabeth Archie, University of Notre Dame, College of Science, Dept. of Biological Sciences

The vertebrate gastrointestinal tract is home to a complex community of microbes that provide a number of "ecosystem services" to its host, such as training the immune system, producing vitamins, resisting pathogens, contributing to host energy acquisition, and allowing hosts to occupy new ecological niches. To date, a lack of prospective, longitudinal data on gut microbial dynamics means we do not yet understand how the gut microbiome changes across an individual's life, or whether these changes serve as bellwethers of individual health, development, and aging. For my PhD thesis, I propose to address this gap using an unprecedented longitudinal data set spanning 19,885 unique freeze-dried fecal samples from 617 known individuals over the course of 15 years. Collected by the Amboseli Baboon Research Project (established 1971), this data has corresponding demographic data, health measures, social interaction data. Because of the unprecedented nature of this baboon gut microbiome dataset, we will be able to understand, for the first time, how the gut microbiome changes over entire lifespans, and whether the gut microbiome exhibits predictable signs of aging. Next, we will test which forces explain inter-individual differences in gut microbial development and aging, focusing on the roles of nutrient limitation and social isolation. Lastly, we will test the roles of gut microbial diversity, composition, and stability on longer term measures of host fitness, such as overall lifespan and reproductive success, thereby testing common but unproven definitions of "healthy" microbiomes. By determining the factors that influence a favorable gut microbiome composition, my results will reveal what constitutes a healthy microbiome across life and thus direct microbiome interventions that efficiently improve human health. This research will also contribute to the field of evolutionary biology by testing the correlation between microbiome composition and markers of Darwinian fitness.

Muropeptide Binding and the X-Ray Structure of the Effector Domain of the Transcriptional Regulator AmpR of *Pseudomonas aeruginosa*

David Dik, College of Science, Jed Fisher, Chemistry and Biochemistry, Lance Hellman, Chemistry and Biochemistry, William Boggess, Chemistry and Biochemistry, Byungjin Byun Chemistry and Biochemistry, Dusan Hesek, Mijoon Lee, Chemistry and Biochemistry, Teresa Domínguez-Gil, Jennifer Fishovitz, Juan Hermoso, Shahriar Mobashery, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

A complex link between cell-wall recycling/repair and the manifestation of resistance to β-lactam antibiotics in many *Enterobacteriaceae* and *Pseudomonas aeruginosa*). This binding selectivity revises the dogma in the field. The crystal structure of the EBD dimer was solved to 2.2 Å resolution. The EBD crystallizes in a "closed" conformation, in contrast to the "open" structure required to bind the muropeptides. Structural issues of this ligand recognition are addressed by molecular dynamics simulations, which reveal significant differences among the complexes with the effector molecules.



Numerical Methods for Modeling Electrostatic Deflections

Kelsey DiPietro, College of Science, Alan Lindsay, University of Notre Dame, College of Science, Dept. of Applied and Computational Mathematics and Statistics

Mathematical models often use partial differential equations (PDEs) to model physical phenomenon. Usually these problems cannot be solved analytically, so we rely on numerical methods to estimate the solution. Numerical methods have been well studied for low order, smooth, lower dimensional problems, but many PDEs exhibit singularities which are challenging to resolve using standard numerical methods, especially for problems in multiple spatial dimensions and with higher order derivatives. We use moving mesh adaptive methods to accurately solve for a singular, high order PDE with a specific application in Micro-Electromechanical systems (MEMS).

MEMS are a family of micro-scale technologies that utilize electrostatic and elastic forces to move their mechanical components on small length scales. MEMS have a variety of applications, ranging from microscopic drug delivery to resonators. A critical component to many MEMS devices is the capacitor, where an elastic top plate is situated above a fixed ground plate. A voltage is applied to the top plate, causing a deformation toward the bottom plate and for large enough voltages, the top plate can make contact with the bottom plate called *touchdown*.

We study two related fourth order PDE models for the capacitor. The first describes the system leading up to a touchdown event, where the amount and location of touchdown points depend on the voltage parameter and the shape of the domain. The second model addresses the system of the behavior after touchdown, where sharp interfaces propagate through the domain until pinned by the boundary. We develop efficient, adaptive numerical methods to accurately solve the model. These methods are robust enough resolve touchdown points as they dynamically evolve as well as the post-touchdown propagating interfaces. To confirm the accuracy of our method, we compare it to existing approximations and observe good matching.

Modeling Podocyte Diseases and Development with Zebrafish

Bridgette Drummond, College of Science, Biological Sciences, Paul Kroeger, College of Science, Gary Gerlach, Wolfram Goessling, Harvard, Ignaty Leshchiner, Harvard, Gary Gerlach, Rebecca Wingert, University of Notre Dame, College of Science, Dept. of Biological Sciences

Specialized renal epithelial cells known as podocytes create a filter in the glomerulus that initiates the process of removing waste from the bloodstream. Podocyte loss is indicative of several types of kidney diseases and can lead to end stage renal disease and kidney failure. Podocyte morphology and genetic regulatory systems are conserved in zebrafish, making them a simplified and accessible model to study podocyte development and disease states. Recently we reported that whole genome sequencing revealed that a splicing mutation in the breast cancer 2, early onset (brca2) gene causes edema and podocyte loss in the zeppelin (zep) mutant. Though brca2 and its mammalian counterpart BRCA2 have not previously been implicated to be a major player in kidney development, morpholino-induced knockdown of brca2 also led to edema and loss of podocytes. Further, histology of zep embryos at 5 dpf, as well as histology of juveniles with an insertional deletion in brca2, also revealed significant glomeruluar defects. In addition, brca2 cRNA injection was sufficient to both partially rescue podocytes in zep mutants and induce ectopic podocyte formation in wild-type embryos. Interestingly, H2AX antibodies showed that zep mutants have disabled DNA repair which suggested that the brca2 protein is also dysfunctional in these animals. We have also performed an ENU screen and identified an additional mutant, ND172, that has a significant loss of podocytes as well as a dramatic decrease in several known renal progenitors such as lhx1a and pax2a. Along with zep, ND172 provides a unique model to assess how an organism complensates with loss of podocytes and provides new insights to genetic factors that lead to a variety of kidney diseases.

An Adaptive Mechanism for Multiple Queries in Differentially Private Data Synthesis

Evercita Eugenio, College of Science, Applied and Computational Mathematics and Statistics, Fang Liu, University of Notre Dame, College of Science, Dept. of Applied and Computational Mathematics and Statistics

In an era where transparency has become of extreme importance, more and more businesses, schools, and government agencies are being asked to publicly release their data. Simply releasing anonymized data though still poses a huge data privacy risk. Intruders may be able to identify subjects in a released data set by exploiting known connections and combining their knowledge with public information. This why when managing data sets that contain sensitive information, it is of utmost importance to properly balance protecting the privacy of individuals who contribute to databases and releasing datasets of good utility.
Differential privacy provides a conceptual approach that brings strong mathematical guarantee for privacy protection. Currently available differentially private data synthesis methods often independently sanitize queries via the Laplace and exponential mechanisms to generate synthetic data with differential privacy ensured. However, since the correlation between queries is unaccounted for, excessive noise may be added to the released results. I will present an adaptive mechanism that uses multiplicative weights to create a distribution that is similar to the true data, based on a specified set of queries. This adaptive mechanism considers the relationship between queries to preserve as much of the original information as possible when releasing synthetic data that ensures differential privacy.

Differential N-Terminal Acetylation of S18 Paralogs by *Mycobacterium marinum* RimI

Micah J. Ferrell[1], Matthew M. Champion[2] and Patricia A. Champion[1]

[1]Department of Biological Sciences, Eck Institute for Global Health, University of Notre Dame, Notre Dame, Indiana 46556
[2]Department of Chemistry and Biochemistry, Eck Institute for Global Health, University of Notre Dame, Notre Dame, Indiana 46556

N-terminal acetylation (NTA) involves the post-translational addition of an acetyl group to the N-terminal amino group of proteins. While this process is ubiquitous in eukaryotes it remains poorly studied prokaryotes. To date only a limited number of prokaryotic NTA proteins have been described however, recent advances in their detection suggest they may be more common than originally thought. Among the few known prokaryotic NTA proteins is the ribosomal structural protein S18 which is acetylated by the N-acetyl transferase enzyme RimI. While the purpose of S18 acetylation remains largely unknown, disruption of this process in *E. coli* has been shown to produce a temperature-sensitive phenotype. Most bacterial species have a single S18 gene however many species of the clinically important genus *Mycobacterium* have been found to possess two S18 paralogs, S18-1 and S18-2. Switching between these alternate S18 proteins is regulated by the availability of zinc with S18-1 used at high zinc levels and S18-2 used when concentrations are low. It has been proposed that this S18 switching and subsequent ribosome remodeling could provide a flexible adaptation to stress. As part of a biochemical screen for N-acetyl transferases we evaluated the RimI enzyme from *M. marinum* (MMAR_1123) for N-acetyl transferase activity towards the N-terminal peptides of S18-1 and S18-2. We found that purified RimI readily acetylates the S18-2 peptide but has no detectible activity towards S18-1 or other non-substrate peptides in our assay. These results suggest that S18-1 and S18-2 undergo different post-translational processing with potential implications for their regulation and ultimate incorporation into the ribosome.

Discovery and Rational Design of Linear Antimicrobial Peptides from a Circular Bacteriocin

Francisco Fields and Shaun Lee, Department of Biological Sciences, University of Notre Dame

Membrane active antimicrobial peptides are linear, alpha helical, cationic, amphipathic linear peptides that defend the host against infection. Traditionally, antimicrobial peptides are designed from naturally occurring peptides from eukaryotes. Therefore, the antimicrobial peptides of bacteria, bacteriocins, represent an underutilized source for the development of linear, membrane active antimicrobial peptides. Using an AS-48 like bacteriocin scaffold, we designed a library of linear peptides to study the role of individual amino acids in optimization of bacteriocin antimicrobial activity.

The AS-48 peptide library was designed by replacing negative and polar amino acids with Lysine and aliphatic amino acids with Tryptophan. Using various bacteria, the peptide library was screened. Peptides with antimicrobial activity were pursued for more detailed studies. Liquid growth assays were used to determine the MIC of the peptide leads against target bacteria. Eukaryotic cytotoxicity was tested using ethidium homodimer and red blood cell lysis assays. Circular dichroism was a used to probe the secondary structure of the peptides. Fluorescent microscopy and FACS sorting using propidium iodide was also used to evaluate the mechanism of action of the peptide. In short, we have identified select peptide leads for further study from our screen.

Our findings indicate that our peptide is a membrane active, amphipathic, helical antimicrobial peptide. Peptide libraries that optimize the charge and hydrophobicity of bacteriocin derived peptides are a useful tool for improving peptide antimicrobial activity. These optimized peptides could be used for the development of novel therapeutics, natural food preservatives, or plant disease control compounds.

Effectiveness of Sub-Therapeutic Staurosporine on Inhibition of Budding and Replication of Lipid-Enveloped Viruses

Mark Fraser, College of Science, Biochemistry, Scott Olehnik, College of Science, Arwa Mohammad, College of Science, Science Preprofessional Studies, Robert Stahelin, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

Infectious Diseases are a major cause of morbidity and mortality internationally, disproportionately affecting developing countries. Many of the deficits caused by infectious diseases are due to viruses, specifically lipid-enveloped viruses. By identifying a common infectious pathway via viral phosphatidylserine (PS) to host TIM protein receptor and a class of drug that was recently found to potentially interfere with this common pathway, it was hypothesized that staurosporines, specifically UCN-01, can inhibit viral infection and replication of lipid-enveloped viruses dependent on viral PS and host TIM receptor interactions, including but not limited to Ebola virus, Marburg virus, HIV-1, Dengue virus, Chikungunya virus, and Zika virus. The effects of UCN-01 on the effects of PS localization in mammalian cells, the effects of UCN-01 on GFP tagged viral matrix proteins in cell culture, and the efficacy of UCN-01 on live virus infected cells are being studied. It was shown using confocal microscopy that UCN-01 is able to significantly reduce plasma membrane localization of both ebola VP40 and HIV-gag proteins in HEK cells. Flow cytometry was also performed on samples under the same experimental conditions showing alterations in external cell membrane PS expression and drug toxicity over a range of concentrations. This pathway was further supported by previous work done in this lab by showing that Ebola VP40 protein induces PS expression in a cell culture model by using confocal microscopy and flow cytometry. By testing UCN-01 to determine cell toxicity using Caspase 3 and MTT assays, how UCN-01 affects cell lipidomics using mass spectrometry, and how effective UCN-01 is at interfering with virus like particle production through virus like particle assays. After showing efficacy at sub-toxic levels in the matrix protein model, live virus studies were initiated and have already shown complete viral infectivity inhibition using low MOIs of Dengue virus using TCID-50 assays. These studies, if successful at decreasing infectivity or viral replication, could lead into future animal model studies that may be taken into clinical trials, producing a broad-spectrum anti-viral therapy that would have the potential to eliminate a large portion of the global health burden.

High-Throughput Multiparametric Scoring of Misfolding Defects in Non-Ketotic Hyperglycinemia

Stefan Freed, College of Science, Shaun Lee, University of Notre Dame, College of Science, Dept. of Biological Sciences

A major challenge facing the advent of truly personalized therapeutics is the difficulty in understanding how a genetic mutation can contribute to disease through disruption of protein folding. Advances in computational modeling of molecular dynamics have allowed new insights into protein structure and function, but are insufficient to predict de novo have a mutation will affect the complex process of biosynthesis and concomitant folding. We have sought to simplify the problem by selecting well-understood biochemical and structural aspects of protein synthesis and function that can impact proper folding and, therefore, cellular function and biostability. These parameters are scored and aggregated to a single number that can be predictive of the likelihood or severity of protein misfolding for any given missense genetic mutation in a protein with a known structure or with sufficient homologous structural data. We have applied this methodology to Non-ketotic Hyperglycinemia (NKH), a rare inborn error of metabolism resulting from deficiencies in the glycine cleavage system (GCS). We have scored all 12,335 possible mutations in the two proteins of the GCS responsible for NKH, including the 207 mutations clinically observed in patients afflicted with NKH, for likelihood of protein misfolding severity. Our scoring approach yields scores are significantly higher for NHK patient alleles than for those observed in healthy patient alleles from the ExAC database, suggesting clinical relevance and potential for prognostic utility. We are in the process of refining the scoring method to better fit biochemical, cellular, and clinical outcomes of GCS mutations, with the aim of producing a tool for patients, physicians, and investigators to use in the study and treatment of NKH as well as other rare diseases.

Commissioning of the High Efficiency Total Absorption Spectrometer (HECTOR)

Orlando Gomez, College of Science, Physics, Shane Moylan, College of Science, Michael Skulski, College of Science, Christopher Seymour, College of Science, Bryant VandeKolk, College of Science, Sabrina Strauss, Doctoral Programs, Physics, Samuel Henderson, College of Science, Farheen Naqvi, Physics, Jack Wurzer, College of Engineering, Craig Reingold, College of Science, Tyler Anderson, College of Science, Artemis Spyrou, Michigan State University, Alicia Palmisano, Michigan State University, Alex Dombos, Michigan State University, Anna Simon, University of Notre Dame, College of Science, Dept. of Physics

In nucleosynthesis, the p-process is responsible for producing several stable neutron deficient nuclei (p-nuclei). The p-process is thought to occur during a Supernova explosion when a shockwave passes through its outer layers prompting a series of photodisintegration reactions: (γ,n), (γ,p), and (γ,α). After the shockwave passes, the unstable nuclei β-decay towards the valley of stability forming stable p-nuclei. Several thousand of nuclear reactions are involved in the p-process, many of which have not been verified experimentally. This leads to large uncertainties in cross sections and reaction rates required for the p-process description, which further leads to conflicting predictions of p-nuclei abundances. The High Efficiency TOtal Absorption SpectrometeR (HECTOR) is a 4π γ-summing detector built and commissioned at the Nuclear Science Laboratory at the University of Notre Dame to measure cross sections of interest for the p-process. Details of the HECTOR design, and results of the commissioning experiments using standard calibration sources and known resonances in the 27Al(p,γ)28Si reaction will be presented.

An Integrative Platform for Three-dimensional Quantitative Analysis of Spatially Heterogeneous Metastasis Landscapes

Ian H. Guldner[1,4], Lin Yang[2,4], Yizhe Zhang[2,4], Fang Liu[3,4], Danny Z. Chen[2,4], Siyuan Zhang[1,4,*]

[1] Department of Biological Sciences, College of Science, University of Notre Dame, Notre Dame, IN 46556, USA
[2] Department of Computer Science and Engineering, College of Engineering, University of Notre Dame, Notre Dame, IN 46556, USA
[3] Department of Applied and Computational Mathematics and Statistics, College of Science, University of Notre Dame, Notre Dame, IN 46556, USA
[4] Mike and Josie Harper Cancer Research Institute, University of Notre Dame, South Bend, IN 46617, USA

Metastatic microenvironments are spatially and compositionally heterogeneous. This seemingly stochastic heterogeneity provides researchers great challenges in elucidating factors that determine metastatic outgrowth. Herein, we develop and implement an integrative platform that will enable researchers to obtain novel insights from intricate metastatic landscapes. Our two-segment platform begins with whole tissue clearing, staining, and imaging to globally delineate metastatic landscape heterogeneity with spatial and molecular resolution. The second segment of our platform applies our custom-developed SMART 3D (**S**patial filtering-based background removal and **M**ulti-ch**A**nnel forest classifiers-based 3D **R**econs**T**ruction), a multi-faceted image analysis pipeline, permitting quantitative interrogation of functional implications of heterogeneous metastatic landscape constituents, from subcellular features to multicellular structures, within our large three-dimensional (3D) image datasets. Coupling whole tissue imaging of brain metastasis animal models with SMART 3D, we demonstrate the capability of our integrative pipeline to reveal and quantify volumetric and spatial aspects of brain metastasis landscapes, including diverse tumor morphology, heterogeneous proliferative indices, metastasis-associated astrogliosis, and vasculature spatial distribution. Collectively, our study demonstrates the utility of our novel integrative platform to reveal and quantify the global spatial and volumetric characteristics of the 3D metastatic landscape with unparalleled accuracy, opening new opportunities for unbiased investigation of novel biological phenomena *in situ*.

A Measurement of the Nuclear Levels in 19Ne using GODDESS

Matthew Hall, College of Science, Physics, Daniel Bardayan, University of Notre Dame, College of Science, Dept. of Physics

A direct way to test nova explosion models is to observe gamma rays created in the decay of radioactive isotopes produced in the nova. One such isotope, 18F, is believed to be the main source of observable 511-keV gamma rays. The main destruction mechanism of 18F is thought to be the 18F(p,α)15O reaction, and the uncertainty in the reaction rate is attributed to uncertainties in the energies, spins, and parities of the nuclear levels in 19Ne near the proton threshold. A 3He beam was used at Argonne National Laboratory in an effort to understand the levels in 19Ne via the 19F(3He,t)19Ne reaction. Gammasphere ORRUBA Dual Detectors for Experimental Structure Studies (GODDESS) was used to measure gamma rays from the decay of 19Ne in coincidence with the reaction tritons. Preliminary data from the experiment will be presented. This research was supported by the National Science Foundation, the US DOE Office of Nuclear Physics and the National Nuclear Security Administration.

Infectious Systems of Uncertainty: The Effect of Partial Observation on Inferences of Epidemiological Parameters

Karlyn Harrod, College of Science, Applied and Computational Mathematics and Statistics, Bryan Greenhouse, University of California San Francisco, School of Medicine, Alex Perkins, University of Notre Dame, College of Science, Dept. of Biological Sciences

Ideally, when building a transmission network to trace the path of how a disease spreads through a population of hosts, one would have complete contact-tracing data. However, in practice, only a portion of the network is observed due to inherent aspects of the methods of collecting contact data. Missing such information could potentially bias inferences made based on contact-tracing data. After simulating a complete transmission network, we used an independent partial observation model to generate partial transmission networks, which assumes that each case is equally likely to be observed. We then used both the full and partial networks to generate estimates of R0 and the dispersion parameter. R0 is the average number of secondary cases that arise from a single infected case and is a metric of how quickly a disease is spreading. The dispersion parameter can be used as a measure of transmission heterogeneity. Estimates of R0 and the dispersion parameter obtained through chain-size distribution analysis, offspring analysis, and joint chain and offspring analysis were similar to the values of R0 and the dispersion parameter that were used to generate the full transmission network, indicating that chain-size data and offspring data could be a valid basis for estimating R0. The estimates obtained using the partial networks and the offspring distribution were slightly higher than the R0 values that were used to generate the networks. However, this increase in R0 can be attributed to the partial observation model in that when a node is deemed "unobserved," its children are assigned to the parent of that node, which then increases the overall number of children for the node's parent. In ongoing and future work, networks will be simulated under different partial observation models to more accurately reflect different assumptions about how case data might be obtained in practice.

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 (1,2), Jing Yang(1,2), Laura Tarwater (1,2), Yuliya Klymenko (2,5), Jeff Johnson (1,2), Zonggao Shi (1,2), Gifty Marfowaa (6), Brooke Kowalski (1) 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, University of Notre Dame, Notre Dame, IN

Ovarian cancer is the most lethal gynecological cancer in U.S. women. Poor 5-year survival rates (<30%) are due to presentation of most women at diagnosis with advanced stage disease with widely disseminated intraperitoneal metastasis. However, when diagnosed before metastatic propagation the overall 5-year survival rate is >90%. Metastasizing tumor cells grow rapidly and aggressively attach to the mesothelium of all organs within the peritoneal cavity, including the parietal peritoneum and the omentum, producing secondary lesions. Mesothelin (MSLN), a 40kDa glycoprotein that is over expressed in many cancers including ovarian and mesotheliomas is suggested to play a role in cell survival, proliferation, tumor progression and adherence. However, the biological function of mesothelin 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 to adhere to the mesothelium of the organs in the peritoneal cavity. An allograft tumor study, using MSLN WT and KO mice injected intraperitoneally with fluorescently-tagged syngeneic murine ovarian cancer cells (ID8-RFP) was performed. Disease progression was evaluated post injection by fluorescent *in vivo* imaging prior to end point dissection (~8 weeks). Abdominal organs were dissected, imaged *ex vivo* and organ-specific tumor burden was quantified by tumor area. Tumor burden was significantly decreased in the liver and omentum of MSLN KO mice compared to MSLN WT mice. The results demonstrate a loss of mesothelial cell-ovarian tumor cell adhesion in the peritoneal cavity of mice that do not express MSLN.

Mechanical Repair of Micro-Lesions in Epithelial Tissues

Jamison Jangula, College of Engineering, Chemical Engineering, Pavel Brodskiy, College of Engineering, Megan Levis, College of Engineering, Chemical Engineering, Jeremiah Zartman, University of Notre Dame, College of Engineering, Dept. of Chemical and Biomolecular Engineering

Microtears of the cell membrane are a common impediment for tissue homeostasis and cell survival. These microtears can result from deviations in osmotic pressure, microbial infections, and external mechanical stresses. Due to the frequency of these occurrences, a robust mechanism for cell membrane repair is essential for cell survival and maintenance of tissue integrity. Consequently, it is critical to understand the underlying principles by which cell membrane healing occurs. However, how cells repair microtears is still poorly understood. In particular, it is unclear how cells and their immediate neighbors coordinate their mechanical properties to repair shared membranes in packed tissues. Ablation of the shared membrane between two adjacent cells results in a qualitatively different healing response compared to that of multicellular wounding. As these cell edge wounds are too small to induce inflammatory responses in the surrounding tissue, healing occurs due to regrowth of the ablated membrane via recruitment of actin, myosin, plasma membrane, and internal vesicles. This recruitment is followed by formation of an actomyosin ring around the wound which contracts, thus facilitating wound closure and directing the healing process. Similarly, actin and myosin are recruited around the plane of division for the construction of the actomyosin ring during cell division. This actomyosin ring contracts until it forms the midbody between two daughter cells, which then forms the beginnings of the membrane boundary between daughter cells. Here, we present the hypothesis that microtear healing responses are an implementation of the mechanical machinery of cytokinesis using a combination of computational and experimental approaches. For this purpose, we have developed a mechanical model that recapitulates tissue response to shared membrane ablation and cell division. This model consists of five tissue level properties; cytoplasmic pressure, cortical stiffness, cellular tight junctions, tricellular tight junctions, and forces generated by the actomyosin ring.

Surface Plasmon Resonance (SPR) and Surface Enhanced Raman Scattering (SERS) Combinded Spectroscopy for Elucidating Protein-Ligand Recognition

Ju-Young Kim, College of Science, Chemistry, Zachary Schultz, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

Elucidating protein-ligand binding has attracted the attention from scientists for a long time due to its a key role in chemical signaling across cellular membranes(1). Surface Plasmon Resonance (SPR) is a one of the advanced techniques to study the mechanism because of its label-free, real-time and surface sensitive (~300 nm) analyzing capability(2). However, the inherent drawback of SPR lies in the interference of non-specific bindings to the outcome signals(3). Here, we suggest a solution for the challenge by combining SPR spectroscopy to surface enhanced Raman scattering (SERS). By combining these two promising technologies, our home built combination spectroscopy provides simultaneous detection of chemical specificity and kinetics of molecular interactions. To that end, a sapphire prism with gold film (50 nm) is used as a SPR platform where flow channel is placed. The metallic film surface is covered with mixed self-assembly monolayer of 11-mercapto 1-undecanol (MUOH) and biotinylated thiol (BT). Streptavidin (STV) attached gold nanoparticles (GNPs) solution is injected into the channel and attached to the monolayer due to strong binding affinity of STV-BT. During the flowing, non-specific binding between STV-MUOH also occurred. When 633 nm p-polarized laser light reflects from the metallic surface at resonance angle, surface plasmon arising on the metallic surface and enhanced Raman scattering from molecular binding. SERS signal is detected by the objectives over the channel, while photodiode simultaneously collects reflected light from the laser and provides SPR curve and sensorgram in time scale. Resulting SERS spectra of specific binding of STV-BT and non-specific binding from unexpected molecules showed evidently different peaks from the similar SPR sensorgram increase, and allowed us to distinguish selective binding information. This successful SPR-SERS simultaneous detection showed that our combined spectroscopy has strong potential to be a useful analysis tool to compensate the limitation of current SPR system. (1) E. Ruoslahti, M. Pierschbacher, Science, 1987, 238, 491-497 (2) P. Abadian, C. Kelly, E. Goluch, Anal. Chem, 2014, 86(6), 2799-2812 (3) H. Nguyen, J. Park, S. Kang, M. Kim, 2015, 15(5), 10481-10510

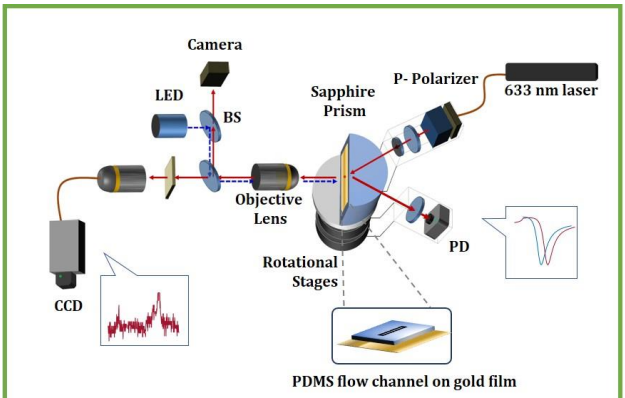


Fig.1 SPR-SERS combined spectroscopy

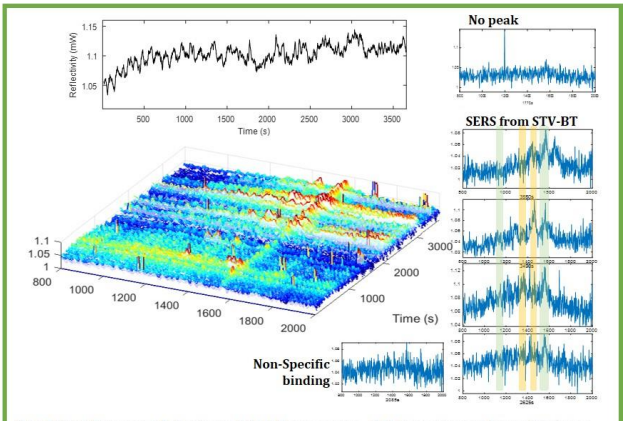


Fig.2 Simultaneous detection of SPR Sensorgram, SERS spectra and specific/ non-specific binding

Cell Surface Expression of the ER-Chaperone Protein GRP78 Regulates Stem Cell and Breast Cancer Cell Migration

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

The molecular chaperone protein GRP78 is generally restricted to the endoplasmic reticulum in normal tissues, where it is a key regulator of the stress response. However, GRP78 has been found to be aberrantly expressed at the cell surface of many types of tumors including breast cancer, where it has been shown to correlate with breast cancer aggressiveness. Interestingly, we have shown that GRP78 is also expressed on the cell surface of induced pluripotent stem cells (iPSCs) and plays an important role in regulating pluripotent stem cell functions. Since numerous studies have found that embryonic mechanisms are present in metastatic cells, understanding how cell surface GRP78 (sGRP78) is achieving these parallel effects in cancer and stem cells could provide important insight into how GRP78 is regulating aggressive breast cancer function. We utilized iPSCs to investigate sGRP78-dependent regulation of stem-like functions that may also be directly applicable to understanding tumorigenesis using cell migration and survival/proliferation assays. It is hypothesized that sGRP78 acts as a peripheral protein on the cell membrane and interacts with other proteins, that vary by cell type, to achieve its functional effects. In order to identify the stem-like specific functions of sGRP78 in breast cancer cells, we used a mass spectrometry and proteomic approach to identify common cell surface binding partners of GRP78 in iPSCs and breast cancer cells. Our lab is investigating Dermcidin as a possible novel sGRP78 binding partner in cancer cells and iPSCs, which could be involved in regulating the oncogenic and stem-promoting effects achieved by GRP78 in aggressive cancer cells and iPSCs. Our data suggests that GRP78 interacts with Dermcidin at the cell surface of cancer cells and iPSCs. We have evidence that this interaction could be important in regulating stem cell and cancer cell migration and survival/proliferation. This work has implications for understanding how cancer cells acquire and exploit stem cell properties, which could provide novel strategies for chemotherapeutic targeting of aggressive stem-like breast cancer cell populations.

Adenomatous Polyposis Coli Regulates Cell Motility through C-Terminal Interactions with the Cytoskeleton

Alyssa Lesko, College of Science, Biological Sciences, Qinfeng Wu, College of Engineering, Maxwell Langer, College of Science, Science Preprofessional Studies, Pavel Brodskiy, College of Engineering, Anna Lyons, College of Science, Jeremiah Zartman, Chemical and Biomolecular Engineering, Jenifer Prosperi, University of Notre Dame, College of Science, Dept. of Biological Sciences

The Adenomatous Polyposis Coli (APC) tumor suppressor is lost in many epithelial cancers. In addition to the well-known function of APC in regulating Wnt signaling, many Wnt-independent functions exist including control of cell migration and cytoskeletal proteins. Our lab made the novel observation that APC knockdown (APC^{KD}) in Madin Darby Canine Kidney (MDCK) cells increased collective cell migration. In the current studies we seek to elucidate the interactions contributing to APC-mediated cell motility by investigating two questions: 1) Does APC loss influence both collective and single cell migration, and 2) Are the same mechanisms responsible for collective and single cell migration? We **hypothesize** that the APC C-terminus regulates collective and single cell migration through cytoskeletal interactions. To investigate APC's role in single cell migration we used time-lapse imaging to track movement of low density MDCK and APC^{KD} cells. Surprisingly, no change was observed in the APC^{KD} cells compared to controls. To investigate the discrepancy between collective and single cell migration, we treated low density cultures with conditioned media to test whether confluent APC^{KD} cells secrete factors that induce migration. While conditioned media enhanced migration in both MDCK and APC^{KD} cells, there were no significant changes between the two. Therefore, current studies will use Ca^{2+} switch experiments to determine if cell-cell contacts are necessary for increased APC-mediated collective cell migration. Next, to identify the important APC binding partners responsible for mediating migration, we assessed the effect of different APC binding domains on cell motility. The APC C-terminus directly binds actin to promote nucleation and assembly. Interestingly the APC C-terminus decreased migration of APC^{KD} cells suggesting the importance of cytoskeletal proteins. A Micropoint laser ablation system was used to cut precise single actin fibers in order to investigate tension. Time-lapse imaging revealed that APC^{KD} actin fibers retract less than control fibers suggesting loss of APC decreases actin fiber tension. Current studies are focused on investigating actin dynamics and retrograde flow during collective and single cell migration. These studies will identify the key cytoskeleton/APC interactions responsible for mediating cell motility allowing future studies to target these interactions as therapies in APC-mutant cancers.

Mechanotransduction in Epithelial Wound Healing

Megan Levis, College of Engineering, Chemical Engineering, Jamison Jangula, College of Engineering, Chemical Engineering, Mark Alber, University of Notre Dame, College of Science, Dept. of Applied and Computational Mathematics and Statistics, and Jeremiah Zartman, University of Notre Dame, College of Engineering, Dept. of Chemical and Biomolecular Engineering

Children can regrow the tip of a finger after an accident, whereas adults cannot [1]. As most tissues age they lose the ability to regenerate and this is replaced by an inflammatory response. This study examines the relationship between the mechanical environment after wounding and the signaling molecules that initiate wound healing. The goal is to understand what causes decreased regeneration with age. Developing wing discs have been previously shown to be a model of a developing tissue that regenerates at an early stage and not later stages. The wing disc tissue was genetically modified with a calcium indicator. Calcium activity in the discs, was measured over the age range of decreased regeneration, showing that calcium activity decreases with age. Correlating decreased baseline calcium activity with decreased regenerative capacity. Then these tissues were wounded to look at the propagation of mechanical tension release through the tissue. Recoil after wounding of the two cell types within the tissue were compared, as an indicator of stress in different parts of the tissue. This second result is being used to calibrate a model of epithelium that was previously developed in collaboration with our lab and Dr. Alber (UC-Riverside). These studies reveal the way the mechanical perturbations of wounding are encoded into the cell and tissue. Understanding the systems involved in healing reveals insight into not only the mechanisms of regeneration but also an understanding of other mechanosensitive processes such as stem cell differentiation and tumorigenesis.

1. McKim LH. CONSERVATISM IN THE TREATMENT OF INFECTIVE BONE LESIONS OF THE FINGERS. Can Med Assoc J. 1930 Nov;23(5):642–644.

The Iroquois Transcription Factor, irx1b, is Required for Proximal Tubule Development in the Zebrafish Kidney

Janice Love, College of Science, Biological Sciences, Rebecca Wingert, University of Notre Dame, College of Science, Dept. of Biological Sciences

The kidney is an essential organ that functions to maintain homeostasis through nutrient reabsorption, waste excretion, and hormone production. These functions are conducted by the nephron, the functional unit of the kidney. The nephron is divided into discrete proximal and distal segments comprised of cells with specific metabolic functions, although the genetic mechanisms underlying the fate decisions that give rise to these cell types is poorly understood. Because nephron segmentation is well-conserved across vertebrate species, including humans, we use the zebrafish embryo as a model to elucidate these unknown genetic mechanisms. Iroquois transcription factors are known to play many roles in developmental patterning, first specifying large territories of tissues before becoming restricted to a subdomain of that territory. Zebrafish have 11 Iroquois transcription factors which previously have been shown to play roles in neuron, cardiac and renal genesis as well. Recently, irx1b was reported in the developing proximal tubule of the zebrafish embryo, suggesting it may have roles in directing segmentation of renal progenitors into the various subdomains of the nephron. Further, transcripts encoding the mammalian orthologue, Irx1, have been spatially localized to growing nephrons in the embryonic mouse kidney. Here, to test the functional requirement(s) of irx1b during nephrogenesis, we performed morpholino-mediated knockdown. Interestingly, irx1b loss-of-function resulted in nephron alterations, where the proximal tubule length was expanded while the distal tubule was reduced. Live imaging of embryos revealed significant alterations in morphology, including pericardial edema, which is indicative of likely fluid-flow and kidney defects, as well as small eyes and the loss of the jaw and the pharyngeal arches. Future studies will examine the expression domain of irx1b in the developing kidney and elucidate the relationships between irx1b and other known nephrogenesis regulators, which can provide new insights into congenital renal defects and other kidney diseases in humans.

Whole-Genome Sequencing and Analysis of Two Burkholderiaceae Members of the Secondary Metabolite-Producing Betaproteobacteria

Daniel Marous, Chemistry and Biochemistry, Mark Horsman, Chemistry and Biochemistry, Shahriar Mobashery, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

We have produced draft WGS sequences of the genomes of two ATCC bacterial strains through collaboration with Notre Dame's Genome CORE facility. We propose reclassification of these strains as Burkholderia and Paraburkholderia members of the betaproteobacteria class. After actinobacteria, betaproteobacteria are the second richest source of bacterial thioester-templated secondary metabolites and often harbor several regulated or cryptically silent pathways. Forty-eight natural product gene clusters are presented from PATRIC (RASTtk) and antiSMASH annotations. While these two isolates are taxonomically distinct at the genome level, they share secondary metabolite pathways not found in their respective genetic nearest neighbours. Initial culturing of both strains suggest one or more of the bioactive end products of these secondary metabolite pathways is expressed and active against Gram-negative bacteria. The assembled genomes provide detailed genetic understanding of the isolate species, the operon regulation elements, and the proteins coded in the putative natural product pathways. These results enable pathway biochemical characterization and strain growth conditioning for the production of these novel compounds. Overall, this work highlights recent advances in bioinformatic prediction tools and second-wave analyses of draft genome-sets, powered by the rapidly expanding set of publicly deposited genomic resources. This approach allows for the identification of novel biosynthetic clusters responsible for microbial production of medically-relevant natural products.

Genetic Mechanisms of Multiciliated Cell Development during Renal Ontogeny

Amanda Marra, College of Science, Meghan Springer, College of Science, Marisa Ulrich, College of Science, Shahram Poureetezadi, College of Science, Rebecca Wingert, University of Notre Dame, College of Science, Dept. of Biological Sciences

Multiciliated cells (MCCs) are found in a wide variety of species and tissues, ranging from the embryonic kidney of frogs and fish to the reproductive and respiratory systems of mammals. Differentiation of MCCs has become an increasingly attractive area of research due to their association with fluid flow and disease. There is evidence for a core, conserved pathway of MCC development that includes the Notch signaling pathway as a negative regulator of MCC fate. The embryonic zebrafish kidney, or pronephros, has emerged as a useful tool to study MCC genesis in vivo, where the transcription factor *mecom* acts upstream of Notch to restrict MCC development while Retinoic Acid (RA) signaling promotes MCC fate by inhibiting *mecom* and promoting expression of the ETS transcription factor *etv5a*. Here, we report phenotype analysis of the allele, which encodes a nonsense mutation in the conserved ETS DNA-binding domain of *etv5a*. Embryos with one copy of this allele display decreased expression of MCCs, suggesting that *etv5a* is a haploinsufficient gene. Next, we found that *mecom* inhibits *etv5a* expression in the kidney, as knockdown of *mecom* caused an expansion of the *etv5a* domain. Further, we uncovered a new role for prostaglandin (Pg) signaling in MCC development. Inhibition of the Pg pathway via Indomethacin or concomitant knockdown of the Pg biosynthesis enzymes Cox1 and 2 significantly reduced MCC number. Interestingly, Pg inhibition did not produce a detectable change in the *etv5a* pronephros domain, suggesting that Pg signaling promotes MCC development separate from *etv5a*. In conclusion, we have discovered a novel relationship between *etv5a* and *mecom* during MCC development, and have identified an essential role for Pg signaling in MCC genesis.

Development of Synthetic Biological Tools for Analytical Applications in Technology Limited Settings

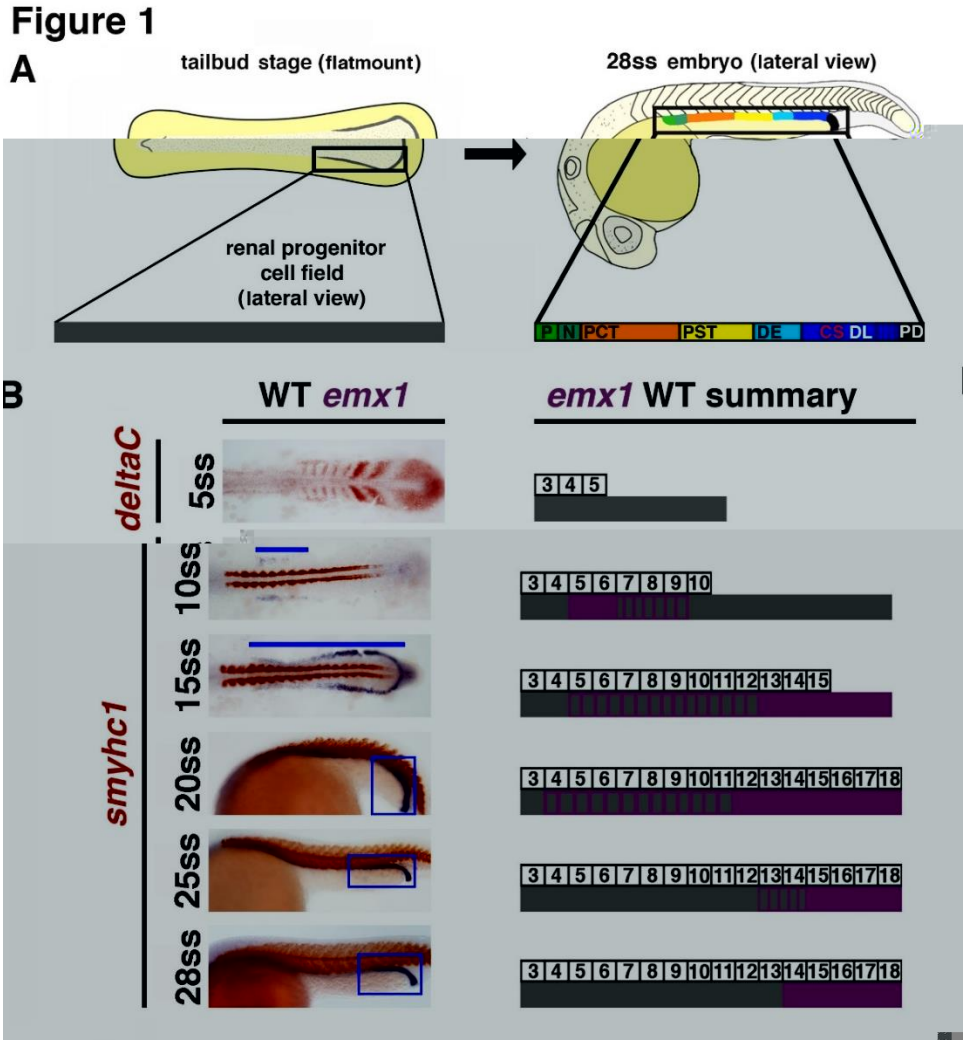
Rachel Miller, College of Science, Marya Lieberman, Chemistry and Biochemistry, Abigail Weaver, College of Science, Biochemistry, Jamie Luther, Biochemistry, Holly Goodson, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

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 developing countries or remote test sites. Paper is a cheap platform for analytical devices. Our lab developed the first paper-based, whole yeast cell biosensor that can detect tetracycline antibiotics over a range of 30 to 10,000 ug/mL. The advent of whole-cell biosensors on paper allows for affordable and field-friendly detection of bioactive contaminants. The long shelf life, durability, and ease of use makes this device ideal for technology limiting environments. We are continuing to develop paper-based whole-cell biosensors to detect chemical compounds that are relevant to analytical problems in low resource settings.

emx1 is Essential for Distal Segment Development in the Zebrafish Pronephros

Elvin Morales, College of Science, Biological Sciences, Rebecca Wingert, University of Notre Dame, College of Science, Dept. of Biological Sciences

Vertebrate kidneys are comprised of functional subunits called nephrons that have three basic parts: a renal corpuscle, a tubule with proximal and distal segments, and a duct. The developmental pathways that establish nephron segment identities from renal progenitors remain poorly understood. The zebrafish is an organism that shares 70% of its genetic code with humans, and its embryos forms a simple two-nephron pronephros that possesses a conserved segment anatomy with higher vertebrates. This, combined with their high fecundity and turnover rate, make the zebrafish an invaluable model to study kidney development. Fully understanding development will help provide a clearer picture of disease onset, as well as improve the production of kidney disease models for the study of renal conditions. For example, using the zebrafish we have begun to uncover essential roles for the empty spiracles homeobox 1 (emx1) gene during renal formation. Using whole mount in situ hybridization, we found that emx1 is dynamically expressed in renal progenitors, and localizes to the caudal domain of the embryonic kidney (Figure 1). Knockdown studies revealed that emx1 is important for nephron patterning, as evidenced by altered distal segments and alterations in the expression of transcription factors critical for distal segment formation. Furthermore, emx1 expression is responsive to changes in retinoic acid (RA) signaling, which is essential to induce proximal segments and repress distal segments during nephrogenesis. Through the continued identification of other components of the gene regulatory networks involving emx1 that direct kidney ontogeny, our research can provide insights into the conserved mechanisms that control renal stem cells and has implications for determining the causes of birth defects.



Purification of Antibodies by Small Molecule-Based Affinity Chromatography via Nucleotide Binding Site

Nur Mustafaoglu, College of Engineering, Chemical Engineering, Basar Bilgicer, University of Notre Dame, College of Engineering, Dept. of Chemical and Biomolecular Engineering and Chemistry and Biochemistry

Antibodies have extraordinary specificity and affinity to antigens, which in turn makes them important candidates to be used in numerous applications including detection, diagnosis, and therapy. Over last two decades, therapeutic antibodies have continued to be evaluated extensively for the treatment of many diseases including cancer and autoimmune diseases. Even though antibody therapies are very efficacious for patients, monoclonal antibody-based treatments are expensive; therefore many patients cannot afford these treatments. A major contributor to the cost of antibody treatments are mostly linked to the downstream production process, or more specifically the usage of Protein A (or G) affinity columns for purification of antibodies. These columns are expensive and have short life cycles with several obstacles that preventing them to be used repeatedly. Here, we designed an affinity chromatography technique for the purification of monoclonal and polyclonal antibodies from cell culture media of hybridomas and ascites fluids. This method utilizes the nucleotide-binding site (NBS) that is located on the Fab variable domain of immunoglobulins to enable capturing of antibody molecules on a membrane affinity column via a small molecule, which has a moderate binding affinity to the NBS. A ring structured small molecule was attached to the resin in order to target the NBS for capturing antibodies on the column. Antibody capture was accomplished by injection of samples while running equilibration buffer (20 mM TRIS pH 7.0) and elution of the antibody was achieved by running a mild elution buffer (0.5 M KCl in 20 mM TRIS pH 7.0). Several pharmaceutical antibodies (IgG), IgE, and Fab were tested on the column, and the results indicate that the column efficiency for antibodies was >98%, with a purity level of >98%. The quality and the capacity of this small molecule membrane affinity purification method is further evaluated for a number of parameters such as: injection concentrations, volumes, wash/bind time, antibody/protein-contaminant combinations, effects of injection buffer, effect of elution buffers, pH, post-purification antigen binding activity of antibodies, and column reusability and stability. This method provides a superior alternative to the protein-A affinity purification method that is widely used for purification of humanized and chimeric antibodies.

Using Stark Shifts to Understand the Driving Forces in Plasmonic Catalysis

Darby Nelson, College of Science, Chemistry, Zachary Schultz, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

In recent years, the optical excitation of plasmon resonances in metal nanostructures has been shown to drive catalytic reactions. These photocatalytic effects have been demonstrated, but the underlying mechanisms behind why the reaction is taking place are unclear. Are the plasmons really driving the reaction or is something else going on at the surface of these nanostructures? Our research aims to understand how plasmons impact surface reactivity. Previous work has shown, through the use of Raman spectroscopy, that metal nanostructure SERS substrates induce a Stark Shift through a process known as optical rectification (using light to convert an AC field to a DC bias). This optical rectification is associated with the excitement of localized surface plasmon resonances (LSPRs) on a SERS substrate. By applying a bias voltage to counteract the shift, the intensity of the electric field produced by these LSPRs can be quantified. The origin of the bias is confirmed through complementary second harmonic generation (SHG), which arises from second order susceptibility similar to optical rectification. Using a reporter molecule to determine electric field strength, a reaction molecule to monitor chemical reactivity, and mapping along the surface with Raman, the LSPR strength on the surface potential can be correlated with possible catalytic activity. These experiments suggest new insights into the mechanism behind plasmon-mediated catalysis.

Quantitative Online Sheath-Flow Surface Enhanced Raman Detection for Liquid Chromatography

Anh Nguyen, College of Science, Chemistry, Monica Schroll, College of Science, Biochemistry, Zachary Schultz, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

Small molecule identification and quantification is essential to realizing the diagnostic potential of systems biology approaches such as metabolomics. Surface enhanced Raman Spectroscopy is an interesting choice of detector for liquid-phase separations because it can provide structural information for analysis and identification of biomolecules. Our lab had demonstrated a high-throughput coupling of capillary LC with SERS (LC-SERS) using an online sheath flow SERS detector. In sheath-flow SERS, hydrodynamic focusing increases analytes interactions with the SERS substrate thus increasing sensitivity significantly. The combination of UV-Vis and SERS detections in series following capillary LC separations in this study provides better limits of detection and chemical information of analytes in mixture compared to the traditional detection methods for LC. Here we will also discuss the ability to detect and quantify analytes over a wide range of concentrations by utilizing both built-in UV-Vis detector in LC system and SERS in flow. A mixture of model metabolites (thiamine, folic acid, and riboflavin) was separated and characterized by UV-Vis and SERS detectors connected in series. Acetonitrile in the mobile phase provided an internal standard enabling quantitative detection across SERS experiments. Our results demonstrate that sheath-flow SERS is provides improved detection of molecules which suggests a complementary technique to identify and quantify small molecules separated by LC and can be run in parallel with MS based method.

Matrix Metalloproteinase-9: A Pharmacological Target to Treat Diabetic Foot Ulcers

Trung Nguyen, College of Science, Biochemistry, Derong Ding, Chemistry and Biochemistry, Mayland Chang, Chemistry and Biochemistry

Chronic wounds are major complications of diabetes. The basis for why the diabetic wound is recalcitrant to healing is not fully understood and there are limited therapeutic agents that accelerate or facilitate its repair. We have identified matrix metalloproteinase (MMP)-8 and MMP-9, in wounds of diabetic mice using an affinity resin that binds exclusively to the active forms of MMPs, coupled with proteomics. Topical treatment with a novel & highly selective inhibitor of MMP-9 (compound ND-336) or ablation of MMP-9 accelerates diabetic wound, indicating that MMP-9 is detrimental to diabetic wound healing. The topical application of ND-336 (a small molecule) enhanced healing by lowering inflammation, and by enhancing angiogenesis and re-epithelialization of the wound, hence reversing the pathological condition. We show that ND-336 has superior efficacy than aclerastide, a drug that failed in clinical trials. Treatment with aclerastide results in upregulation of MMP-9. We now report the discovery of (R)-ND-336 , a more potent inhibitor of MMP-9 and better at accelerating wound healing than racemic of ND-336. Becaplermin, the only FDA-approved drug, can lower MMP-9 levels while promoting wound healing in a diabetic mice study, in which (R)-ND-336 indicates to be more efficacious than becaplermin. Furthermore, we identified and quantified active MMP-8 and MMP-9 in wounds of patients with diabetic foot ulcers. There are higher levels of active MMP-9 in patients with chronic wounds than in acute wounds, indicating that the mechanisms of pathology and repair are similar in diabetic mice and diabetic humans.

Disentangling the Relative Roles of Importation and Weather in Driving Interannual Variation in Dengue Epidemics in Guangzhou, China

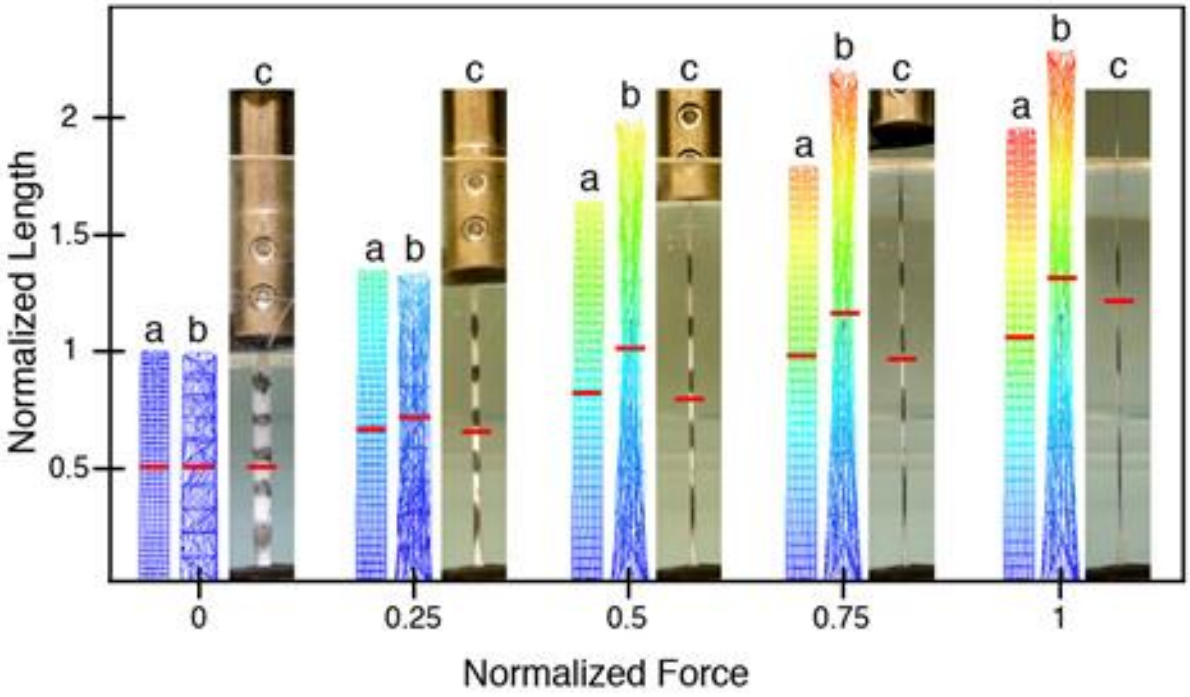
Rachel Oidtman, College of Science, Biological Sciences, Zhoujie Huang, Division of Infectious Diseases, Key Laboratory of Surveillance and Early-warning on Infectious Disease, Center for Disease Control and Prevention, Shengjie Lai, Division of Infectious Diseases, Key Laboratory of Surveillance and Early-warning on Infectious Disease, Center for Disease Control and Prevention; Department of Geography and Environment, University of Southampton, Yu Li, Division of Infectious Diseases, Key Laboratory of Surveillance and Early-warning on Infectious Disease, Center for Disease Control and Prevention, Robert Reiner, Institute for Health and Metrics and Evaluation, University of Washington, Andrew Tatem, Department of Geography and Environment, University of Southampton; Flowminder Foundation, Hongjie Yu, Division of Infectious Diseases, Key Laboratory of Surveillance and Early-warning on Infectious Disease, Center for Disease Control and Prevention, Alex Perkins, Department of Biological Sciences and Eck Institute for Global Health, University of Notre Dame

In 2014, the city of Guangzhou, China experienced a dengue virus epidemic with nearly 40,000 locally transmitted, symptomatic cases. Prior to 2014, the average number of locally transmitted cases was less than 300. To determine whether interannual variation in dengue virus importation or weather conditions might have driven this unusually large epidemic, we incorporated weather data, mosquito trap data, and imported case data from 2005-2015 into a dynamic transmission model. First, we integrated a mechanistic description of weather data and imported case data from the time series into several model iterations, and we compared those simulated data against observed case numbers. Informative lagged weather effects were identified, including average temperature and relative humidity. We then performed a second iteration of model fitting in which we estimated model parameters under a Bayesian framework, specifically to describe uncertainty in lagged weather and mosquito effects and other transmission parameters. We used adaptive Markov chain Monte Carlo methods to estimate the joint posterior distribution of these parameters. By performing simulations with our fitted stochastic model, we were able to show that this model was generally capable of reproducing seasonal patterns of transmission. However, simultaneously reproducing both the full extent of the 2014 epidemic and much lower levels of transmission in several years preceding was more challenging. We ranked epidemic size in each year for each simulation, to determine the probability that a given year had a given rank. Our results showed that 2013 and 2014 were consistently ranked as the two years with the highest dengue incidence. Though our model was able to recreate similar transmission patterns, we were not able to recreate similar transmission magnitude. For these reasons, we concluded that there are likely additional factors beyond imported cases and weather that are necessary to explain the full extent of interannual variation in dengue epidemics in Guangzhou.

Micro-scale Computational Model of Fibrin Networks Mechanics

Francesco Pancaldi, College of Science, Applied and Computational Mathematics and Statistics, Oleg Kim, Department of Mathematics, University of California, Riverside, Mark Alber, University of Notre Dame, College of Science, Dept. of Applied and Computational Mathematics and Statistics

Structural and mechanical properties of fibrin networks, which are essential factors determining growth and stability of blood clots, can dynamically undergo fast changes due to blood flow shear, clot contraction, or vasospasms. Predicting these alterations using computational modeling is important for understanding mechanisms governing clot deformation under various (patho-)physiological conditions and designing new fibrin-based bio-materials. In this talk, a discrete worm-like-chain model (WLC) of a fibrin network is introduced to study how the macro-scale behavior of the network, including macro-scale structural changes and force-strain response of the fibrin clot, emerge from the micro-scale characteristics of the network. The model was calibrated using confocal microscopy data on single fiber stretching and the simulation results will be shown to be in good agreement with the data obtained in the fibrin gel stretching experiments. Additionally, simulations demonstrate how structural metrics, such as length and orientation of individual fibers, change when stretching forces are applied to the network and how network's stress-strain response depends on these metrics. Lastly, the addition of a modeling component representing bending of single fibers, allowed us to study impacts of shear stress and compression on the network and how its stress-strain profile under these conditions depend on bending stiffness and other properties of the network. The suggested micro-scale mechanisms based on alignment and bending of fibers, tested in simulations, are used to make predictions about the behavior of the fibrin network under patient specific conditions.



Homotopies for Overdetermined Systems with Applications in Computer Vision

Margaret Regan, College of Science, Applied and Computational Mathematics and Statistics, Sameer Agarwal, Applied and Computational Mathematics and Statistics, Jonathan Hauenstein, University of Notre Dame, College of Science, Dept. of Applied and Computational Mathematics and Statistics

Many problems in computer vision are represented using a parametrized overdetermined system of polynomials which must be solved quickly and efficiently. We propose new numerical algebraic geometric methods to efficiently solve parameterized overdetermined systems in projective space with the new approaches using locally adaptive methods and sparse matrix calculations. Examples will be provided to compare the new methods with traditional approaches in numerical algebraic geometry.

Extracting Statistical Properties of Samarium Isotopes Using the Oslo Method

Craig Reingold, College of Science, Physics, University of Notre Dame, College of Science, Dept. of Physics, M. Guttormsen, A.C. Larsen, C.W. Beausang, J.T. Burke, Anna Simon, University of Notre Dame, College of Science, Dept. of Physics

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 reactions cross sections can be treated as averaged functions, calculated using statistical factors. These factors include the nuclear level density (NLD) and γ-strength function (γSF).
Providing experimental constraints for the NLD and γSF for samarium isotopes is of utmost importance to nuclear astrophysics, nuclear security, and nuclear structure. Since many reaction cross sections 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 γSF at γ-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 γ-ray scattering in segmented detectors.
In this work, the NLD and γSF 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 γ-ray energies. Particle-gamma coincidence provide correlation matrices of excitation energy vs γ-ray energy, for which the Oslo method is employed to simultaneously extract the NLD and gSF. This analysis has been completed for 152,154Sm(p,d)151,153Sm reactions. In the future, we plan to analyze data from the (p,d) and (p,t) reaction channels of 148,150,152,154Sm and 160Dy.

Dye-Loaded Core-Shell Au-SiO_2 Nanoparticles for Cancer Theranostics

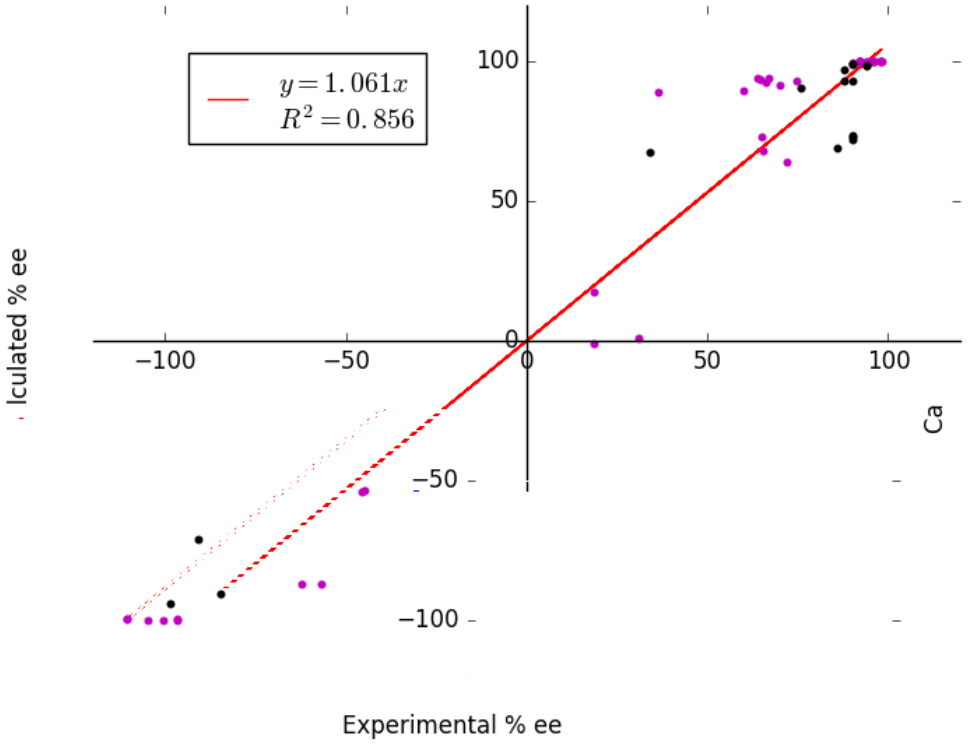
Felicia Roland, College of Science, Qiwei Zhang, Chemistry and Biochemistry, Ryan Roeder, University of Notre Dame, College of Engineering, Dept. of Aerospace and Mechanical Engineering and Bradley Smith, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

Many conventional cancer treatments are generally effective against early stages of cancer, which is problematic because diagnoses are typically made at advanced stages. Therefore, early detection and efficient treatment is essential for improving patient outcomes. One solution to this problem is the development of personalized treatment regimens that combine both, a therapeutic and a diagnostic agent into a single platform, termed "theranostics". Presented here is a core-shell Au-SiO_2 theranostic nanoplatform that contains a novel heat-generating croconaine dye as a therapeutic agent for photothermal therapy (PTT) and gold core for computed tomography (CT) cancer detection. Core-shell nanoparticles were made using novel synthetic method and a silane-functionalized croconaine dye for covalent incorporation into the silica shell. The Au-SiO_2-Croconaine nanoparticles (NPs) exhibit exceptional photophysical properties and robust laser-induced photothermal heating to temperatures that are capable of killing cancer. By covalently modifying the silica shell with the cancer-targeting peptide RGD, these nanoparticles can target integrin $\alpha_V\beta_3$, which is overexpressed in many types of ovarian cancer. The ultimate goal is to use Au-SiO_2-Croconaine NPs for image-guided surgery. After targeted accumulation of the nanoparticles at the tumor site, CT imaging can be used to reveal information about the location and disease state. A surgeon can then perform subsequent tumor removal with the aid of a laser for photothermal therapy to kill tumor microfoci.

Development and Application of the Q2MM Method to Metal and Enzyme Catalyzed Reactions

Anthony Rosales, College of Science, Eric Hansen, College of Science, Per-Ola Norrby, Paul Helquist, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry and Olaf Wiest, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

Reaction specific transition state force fields (TSFF) combine the accuracy of quantum mechanics calculations with the speed of classical force fields and can be derived using the quantum guided molecular mechanics (Q2MM) method that we have developed. This method involves defining new parameters of an existing FF (e.g. MM3) to describe interactions of a TS, and then fitting new parameters to ab initio data generated from QM optimized structures. This work describes the further development of the Q2MM method to enzyme catalysis along with TSFF's that were produced for two reactions of high synthetic and mechanistic interest: Heck arylation/alkenylation and transfer hydrogenation. The large number of residues associated with enzymes has to be considered when trying to describe the potential energy surface of enzymes. Traditional FFs and TSFFs can provide chemical accuracy and sufficient sampling techniques. This work will discuss and address the problems associated with how empirical data along with QM data can be used to sufficiently describe enzyme catalysis and atomic-level detail. Depending on the substrate, the asymmetric Heck reaction has stereoselectivity along with regioselectivity. The Heck TSFF's have demonstrated accurate computed differences of energies (R^2 > 0.8 as shown in figure) for the different diastereomeric transition states, including a di-, tri- and, tetra-substituted alkene substrates. The TSFF developed for transfer hydrogenation is the most general TSFF developed from Q2MM while still retaining diastereomeric accuracy. This unified TSFF was parameterized to simple transition states with Ru, Rh, and Ir. Beyond typical ligand/metal complexes, the TSFF performs similarly with tethered arenes and osmium complexes. Due to the similarities in the H-donor/catalyst and substrate/catalyst TS's, the TSFF can also provide mechanistic insight such as reversibility of some intermediate steps.



Combination of Capillary Electrophoresis and Sheath Flow SERS for Metabolite Detection in Biological Fluids

Emily Shangle, College of Science, Zachary Schultz, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

Biological fluids are highly complex samples that contain an abundance of medically relevant information. Being able to detect and identify low level metabolites in these samples without pretreatment or expensive equipment would be an attractive diagnostic tool. Surface-enhanced Raman scattering (SERS) is a sensitive spectroscopy technique that allows for label-free molecular specific identification. Our lab uses sheath flow SERS to concentrate analytes onto a silver nanostructure substrate where the SERS signal will be generated. The combination of capillary electrophoresis and sheath flow SERS enables high resolution separation and detection of low level metabolites in biological samples and fluids without pretreatment. Previously, our lab detected low level biological species, such as biologically-active peptides, using a custom capillary electrophoresis sheath flow SERS set-up. We have extended the capabilities of this instrument for the separation of untreated and unlabeled metabolites in urine and serum. Our work suggests that capillary electrophoresis coupled with SERS detection could be a novel platform for biomedical diagnostics.

Exceptional Stewart-Gough Platforms and Segre Embeddings

Samantha Sherman, College of Science, Applied and Computational Mathematics and Statistics, University of Notre Dame

Stewart-Gough platforms are robots made up of a base and platform connected by six legs of fixed length. A generic Stewart-Gough platform is rigid whereas exceptional Stewart-Gough platforms have self-motion. This poster will focus on a family of exceptional Stewart-Gough platforms, called Segre-dependent Stewart-Gough platforms, which arise from a linear dependence among point pairs under the Segre embedding.

Estimating the Population at Risk of Zika in the Asian Region

Amir S. Siraj and T. Alex Perkins, Department of Biological Sciences and Eck Institute for Global Health, University of Notre Dame, Notre Dame, IN USA

On November 18, 2016, the World Health Organization ended its designation of Zika virus (ZIKV) as a Public Health Emergency of International Concern (PHEIC). At the same time, ZIKV transmission continues in Asia, with the number of Asian countries reporting Zika cases increasing over the last two years. Applying a method that combines epidemiological theory with data on epidemic size and drivers of transmission, we characterized the population at risk of ZIKV infection in 15 countries in Asia. Projections made under the assumption of no pre-existing immunity suggest that up to 785 (range: 730–992) million people in Asia could be at risk of ZIKV infection under that scenario. Assuming that 20% of ZIKV infections are symptomatic, this implies an upper limit of 146-198 million for the population at risk of a clinical episode of Zika. Due to limited information about pre-existing immunity to ZIKV in the region, we were unable to make specific numerical projections under a more realistic assumption about pre-existing immunity. Even so, combining numerical projections under an assumption of no pre-existing immunity together with theoretical insights about the extent to which pre-existing immunity may lower epidemic size, our results suggest that the population at risk of ZIKV infection in Asia could be substantially larger than in the Americas. As a result, we conclude that the WHO's removal of the PHEIC designation for Zika virus should not be interpreted as an indication that the threat has subsided.

Ca2+ Dynamics in Epithelial Networks

Dharsan Soundarrajan, College of Engineering, Jeremiah Zartman, University of Notre Dame, College of Engineering, Dept. of Chemical and Biomolecular Engineering

Chronic wounds affect around 6.5 million Americans annually. It is claimed that around $25 billion is spent annually in treating chronic wounds. This cost is projected to increase in the future due to the increase in health care costs and increase in the occurrence of diseases such as diabetes. Wound healing is a complex biological process that is conserved and aids all organism to cope with injuries when tissue integrity is damaged. Damaging the tissue microenvironment leads to the release of chemical signals responsible for triggering biochemical pathways that helps restore tissue integrity. Recently, studies in Drosophila wing imaginal discs have shown that Ca2+ is a major regulator of various biochemical pathways involved in wound healing. Furthermore, Ca2+ acts as an inductive signal that originates near the wound edge after an injury and diffuses via gap junctions to the neighboring cells. However, it is unclear as how the tissue architecture defined by cell geometry and cell packing impacts Ca2+ signaling dynamics. To systematically understand the interplay between altered tissue architecture and Ca2+ signaling, we have developed a cell based computational model. Our results from our modeling studies shows that changes to tissue topology following injury affects the spatiotemporal patterning of Ca2+ near the wound site. The results from this study implies that the changes to normal cell architecture, which frequently accompanies chronic diseases, affects the spatiotemporal patterning of the inductive signal which could potentially result in a poor wound healing outcomes.

Synthesis and Biological Studies of the Cinnamonitrile Class of Molecules as Antibiotic Potentiators for Methicillin-Resistant *Staphylococcus aureus* (MRSA)

Enrico Speri, College of Science, Biochemistry and Chemistry, Choon Kim, Chemistry and Biochemistry, Elena Lastochkin, Chemistry and Biochemistry, Mayland Chang, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry and Shahriar Mobashery, University of Notre Dame, College of Science, Dept. of Chemistry and Biochemistry

Antimicrobial resistance is one of the most serious threats to global public helath today. β-Lactam antibiotics were the preferred antibiotics for treatment of infection by Staphylococcus aureus, but emergence of Methicillin-resistant *Staphylococcus aureus* (MRSA) in 1961 made these drugs obsolete within a short time. In response to exposure to β-lactam antibiotics, MRSA exhibits phosphorylation of certain proteins. Interference with phosphorylation reverses the antibiotic-resistance phenotype. We describe the cinnamonitrile class of molecules that are capable of this phenotype reversal, restoring sensitivity to the organism against β-lactam antibiotics.

Exploring the Aging of MoS¬2 through Ambient Pressure X-ray Photoelectron Spectroscopy

Subha Subha, Physics, Weixin Huang, College of Science, Sylwia Ptasinska, University of Notre Dame, College of Science, Dept. of Physics

The discovery of two-dimensional layered semiconducting transition metal chalcogenides (TMD) has produced enormous attention both in industry and scientific research owing to their unique material properties including weak van der Waals interactions, sizable intrinsic bandgap energies, etc. Molybdenum disulfide (MoS2), a well-studied TMD composed of weak van der Waals bonded S-Mo-S units with a band gap, which varies from 1.2 to 1.8 eV transitioning from bulk to single layer, make this material a promising candidate for various optoelectronic applications such as transistor, photodetector and so on. Similar to other low dimensional semiconductors, MoS2 is likely to be highly sensitive to external chemical environment which can affect the functional properties, therefore the MoS2–based devices performance. Thus, in this work, we studied the aging of MoS2 by investigating the interaction of water molecules with a MoS2 surface using ambient pressure X-ray photoelectron spectroscopy (APXPS). Our results revealed the degradation of MoS2 layers after introduction of water vapor at different pressures ranging from 0.1 to 5 mbar. The S to Mo ratio increased from 2 to 2.5 from the fresh sample to aged one, indicating the change in stoichiometric ratio. The peak features corresponding to Mo (+6) oxidation state was also observed which confirmed surface oxidation. The morphological changes of the MoS2 surface with introduction of water vapor were also observed through scanning electron microscopy (SEM). Our study indicates poor water stability of MoS2 which is undesirable for fabricating field effect transistors and other related electronic device architecture.

Multiple Pathways Activate Cip1 to Inhibit Cd 1 **k1-G1 Cyclins upon Stress**

Chien-Wei Wang, Department of Microbiology, College of Medicine, National Taiwan University, Taipei, Taiwan, College of Science, Shu-Chun Teng, National Taiwan University

Environmental stress, such as osmotic stress, triggers the G1 progression delay of *Saccharomyces cerevisiae* to prevent damage accumulation. Cip1, **C**dk1 **I**nteracting **P**rotein, has known to associate with Cdk1 (Cyclin-dependent kinase 1) and Cln2. However, the role of Cip1 in regulating cyclin-dependent signaling pathways is still poorly understood. Our data suggest that Cip1 expression is co-regulated by the cell cycle-mediated transcriptional factor Mcm1 and the stress-mediated transcriptional factors Msn2/4. Overexpression Cip1 inhibit all Cdk1-G1 cyclin complexes therefore arrest cells in the G1 stage. Moreover, a stress-activated protein kinase phosphorylates Cip1 to strengthen the interaction between Cip1 and Cdk1/G1 cyclin complex. These results indicate that stress-induced Cip1 phosphorylation inhibit the Cdk1/G1 cyclin pathway to delay early G1 progression. We proposed that Cip1 and Sic1, the major stress-induced CDK inhibitor, are functionally redundant in causing transient G1 delay under osmotic stress.

Unprecedented Eukaryotic Gut Microbiome Diversity is Governed by Conserved Ecological Processes in a Non-Human Primate

Justin Wilcox, College of Science, Biological Sciences, Hope Hollocher, University of Notre Dame, College of Science, Dept. of Biological Sciences

The majority of eukaryotic diversity has been suggested to occur on or in other organisms, but the diversity and ecology of symbiotic eukaryotes remains consummately uncharacterized, particularly in contrast to prokaryotic microbiomes. Nonetheless, the keystone roles played by eukaryotes in free-living systems and the ubiquity of parasitism, commensalism, and mutualism, suggest that symbiotic eukaryotes may be important components of host-associated communities. Here, we utilize an Illumina sequencing approach to characterize eukaryotic diversity within the feces of *Macaca fascicularis* (long-tailed macaques) on two islands in South-East Asia: Singapore and Bali, Indonesia. We report levels of eukaryotic diversity higher than previously reported and comparable to free-living ecosystems. Moreover, taxa representing all eukaryotic supergroups occurred universally across samples. Although functional guilds were consistently represented across samples, taxa composition was fluid and covaried in accordance with trophic relationships, suggesting that symbiotic eukaryotic communities may be governed by the same ecological principles as free-living systems. Overall, our results suggest that vertebrates may host a vast reservoir of hidden eukaryotic diversity, and highlight potentially critical roles for this eukaryotic diversity in the community ecology of primate microbiomes.

Intercellular Calcium Waves are Controlled by Morphogen Signaling during Organ Development

Qinfeng Wu, College of Engineering, Megan Levis, College of Engineering, Chemical Engineering, Cody Narciso, College of Engineering, Chemical Engineering, Pavel Brodskiy, College of Engineering, Jeremiah Zartman, University of Notre Dame, College of Engineering, Dept. of Chemical and Biomolecular Engineering

Spontaneous and dramatic intercellular calcium waves are frequently observed during organ development, but are poorly understood. Calcium ions are ubiquitous second messengers that carry out a wide-range of functions, including the regulation of cell proliferation, metabolism and death. Consequently, regulation of calcium signaling encodes a significant portion of the cellular decision making state of cells through both amplitude and frequency-dependent regulation of transcription factors and key regulatory enzymes. Here we report that intercellular calcium waves exhibit spatiotemporal patterns at the organ-level using a quantitative image analysis pipeline. Intercellular calcium waves in the Drosophila wing disc require a specific phospholipase C, Plc21C. Further, we demonstrate that the morphogen signaling pathway, Hedgehog, controls frequencies of calcium oscillations uniformly in the tissue and is required for non-uniform spatial patterning of oscillation amplitudes. Thus, the dynamics of spontaneous intercellular calcium waves are regulated by morphogenetic signaling. Intercellular calcium waves propagate information at the organ-scale that reflects the differentiation state of the developing wing disc.

Generation of Induced Pluripotent Stem Cells from Acute Myeloid Leukemia

Amanda Yamasaki, College of Science, 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 a defect in hematopoietic differentiation that leads to the accumulation of immature myeloid cells in affected patients. Unfortunately, although AML is a complex disease that can present with a wide variety of genomic aberrations affecting prognosis, standard course of therapy is virtually identical for all cases – cytotoxic chemotherapy that leads 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 treatment mechanisms. To this end, we have reprogrammed both 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 use of reprogramming as a therapeutic approach in the treatment of diseases with a genetic basis, without relying on complicated gene editing processes, suggesting that in the future, autologous HSC transplants may become a 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 may provide a useful tool to study the development and progression of AML.

Loss of MTSS1 Results in Increased Metastatic Potential in Pancreatic Cancer

Ann Zeleniak, College of Science, Biological Sciences, Mary Brinkman, College of Science, Wei Huang, Biological Sciences, Melissa Fishel, Indiana University School of Medicine, 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 prognosis is largely due to the inability to diagnose the disease before metastasis occurs. Tumor cell dissemination occurs early in PDAC. While it is known that inflammation facilitates this process, the underlying mechanisms responsible for this progression have not been fully characterized. Here, we functionally test the role of metastasis suppressor 1 (MTSS1) in PDAC. Despite evidence showing that MTSS1 could be important for regulating metastasis in many different cancers, its function in PDAC has not been studied. Here, 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. Finally, overexpression of MTSS1 in PDAC cell lines leads to a loss of migratory potential in vitro and an increase in overall survival in vivo. Collectively, our data provide insight into an important role for MTSS1 in suppressing tumor cell invasion and migration driven by the tumor microenvironment and suggest that therapeutic strategies aimed at increasing MTSS1 levels may effectively slow the development of metastatic lesions, increasing survival of patients with PDAC.