2017 Postdoc Research Symposium

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Presentation Abstracts

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1. Isaac M. Adjei

Department: Biomedical Engineering
College: Engineering

Nano-based Approach to Treat Bone Metastasis and Promote Repair of Associated Lost Bone

Co-Authors: Vinod Labhasetwar, Blanka Sharma

Abstract:

Background: Bone metastasis is common in different cancers, and increases morbidity and mortality. The goals of this study were to develop nanoparticles (NPs) to treat bone metastasis, and advance mesenchymal stem cell (MSC)-based repair of lost bone by enhancing osteogenesis and enabling image guided cell implantation and longitudinal monitoring.

Methods: Nanoparticles were formulated from poly-(lactic-co-glycolic)-acid (PLGA-NP). Biodistribution of NPs after intravenous injection was evaluated in a murine model of bone metastasis by fluorescent imaging. Efficacy of paclitaxel-loaded NPs at treating bone metastasis was determined by bioluminescence imaging and micro-CT. For bone repair, PLGA-NPs encapsulating resveratrol (RESV) to promote osteogenesis were modified with iron oxide NPs, a contrast for photoacoustic tomography and MRI (RESV-NP). Differentiation of MSCs in response to RESV-NP was determined using standard protocols. Photoacoustic imaging of hydrogels encapsulating RESV-NP loaded MSCs was performed in rats.

Results: PLGA-NPs accumulated preferentially in bone metastasis. When loaded with paclitaxel, the NPs inhibited the growth of established bone metastasis and prevented bone loss. To repair bone loss due to metastasis, MSCs pre-loaded with RESV-NP increased mineralization by 27% and 45% compared to supplementation with RESV-NP and free RESV. In hydrogels, RESV-NP loaded MSCs increased the amount and homogeneity of mineralization compared to other groups. RESV-NP loaded MSCs were detected by photoacoustic tomography with resolution of 800 cells/µL which ensured imaging of hydrogel-encapsulated MSCs in rats even after osteogenesis.

Conclusion: We have developed NPs that treat bone metastasis and improve MSC-based bone repair. These NPs have the potential to improve cancer treatment.

2. Derek B. Archer

Department: Applied Physiology and Kinesiology
College: Health and Human Performance

Creating a High-Resolution Descending Motor Template Using Human Connectome Project Data

Co-Authors: David Vaillancourt, Stephen Coombes

Abstract:
The purpose of this study was to develop a high resolution human descending motor area tract template (DMATT) which segments the descending motor tracts based on six cortical regions in primary motor cortex, (M1), dorsal premotor cortex (PMd), ventral premotor cortex (PMv), supplementary motor area (SMA), pre-supplementary motor area (preSMA), and primary somatosensory cortex (S1) using diffusion tensor imaging (DTI). Individual probabilistic tractography analyses were conducted in 100 subjects using the highest resolution data currently available.

Tractography results were refined using a novel algorithm to objectively determine slice level thresholds that best minimized overlap between tracts while simultaneously preserving tract volume. Our observations show that cortical topography is generally preserved as the tracts descend through the brain, with the preSMA tract remaining most anterior and the S1 tract remaining most posterior. Here, we combine our results into a freely available white matter template, named the DMATT. We also provide a probabilistic DMATT that quantifies the extent of overlap between tracts. Finally, we assess how the DMATT operates in individual subjects from the Human Connectome Project as well as individual subjects from another independent dataset.

This DMATT and probabilistic DMATT provide new tools that segment and label descending motor tracts at a spatial resolution not previously available.

3. Soo Jin Jeon

Department: Large Animal Clinical Sciences
College: Veterinary Medicine

Blood microbiota as a potential seeding source for bacteria that cause uterine disease in cows

Co-Authors: Federico Cunha, Achilles Vieira-Neto, Rodrigo C. Bicalho, Svetlana Lima, and Klibs N. Galvão

Abstract:
Background: The uterine microbiota plays an important role in the development of uterine disease. However, the origin of uterine microbiota remains unknown. Here, we hypothesized that bacteria originating from the gut can be translocated to the uterus via the bloodstream. We compared bacterial communities from blood, feces, and uterine samples from the same cows at 0 and 2 days postpartum using deep sequencing and qPCR.

Results: Uterine bacterial communities were more similar to fecal bacterial communities than blood bacterial communities based on the presence and absence of community composition. However, core genera were shared by all blood, feces, and uterine samples. Uterine pathogens such as Bacteroides, Porphyromonas, and Fusobacterium, showed a strong and significant interaction with each other in the network of blood microbiota, but not in feces. The copy number of total bacteria was higher in feces than in blood and uterus. In contrast, copy numbers for Bacteroides heparinolyticus and Fusobacterium necrophorum, which are known uterine pathogens, were more abundant in the uterus than in blood and feces.

Conclusions: Our findings suggest that the gut can be a source of uterine infection and specific bacteria are more capable of invading and colonizing the uterus, thereby causing uterine diseases. In particular, microbial interactions in blood may be an important component of disease etiology. This study shows the feasibility of hematogenous spread of uterine pathogens in cows, but a similar mechanism may be present in other mammals, and deserves further investigation.

4. Sarah A. Johnson

Department: Neuroscience
College: Medicine

Older adult rats also forget where they parked their cars: animal models for stimulus discrimination and age-related memory loss

Co-Authors: Sean M. Turner, Andrew P. Maurer, Jennifer L. Bizon, Sara N. Burke

Abstract:
Background: Loss of detailed memory for similar, recurrent events is a common symptom of aging. This ability to distinguish between overlapping episodes, such as daily locations of your parked car, is thought to require complex stimulus discrimination. Recent studies in elderly humans have confirmed stimulus discrimination impairments correlate with episodic memory decline, yet there is a need for animal models of these deficits to investigate their neurobiological underpinnings. We therefore asked whether impaired discrimination of similar stimuli is observed in a rodent model of aging.
Methods: Young adult (4-6 months) and aged (24-28 months) F344 x Brown Norway hybrid rats were trained to distinguish between pairs of spatial locations or three-dimensional objects. Rats were then tested for their ability to discriminate between distinct versus similar stimuli. Similarity of locations and objects was systematically varied by increasing overlapping visual features shared across stimulus sets.
Results: Aged rats were impaired when discriminating similar stimuli that shared many features, but performed on par with young when discriminating distinct stimuli. Age-related deficits were observed across cognitive modalities; aged rats had trouble discriminating both similar spatial locations and similar objects.
Conclusions: Our major finding is that, in rats, age-related impairments in distinguishing between similar stimuli directly parallel those observed in humans. This demonstrates validity of our model for refining stimulus discrimination tasks as neuropsychological screening tools, and for investigating neurobiological mechanisms that contribute to age-related memory loss. Our discrimination tasks may also prove useful in screening potential therapeutic interventions for dementias and Alzheimer’s disease.

5. Carla Mavian

Department: Pathology, Immunology and Laboratory Medicine
College: Medicine

Emergence of recombinant Mayaro virus strains from the Amazon basin: the dawn of a new epidemic?

Co-Authors: Brittany D. Rife, James Jarad Dollar, Eleonora Cella, Massimo Ciccozzi, Mattia C. F. Prosperi, J Glenn Morris Jr, Ilaria Capua, Marco Salemi

Abstract:

Background: Mayaro virus (MAYV), the causative agent of Mayaro fever, is an arbovirus transmitted by the Haemagogus species of mosquito endemic to the Amazonian forest in South America. Despite its role in a highly debilitating disease and recent evidence of spread areas outside of the Amazonian regions of Central and South America, limited information about the evolution and the epidemiology of MAYV represent an important barrier to prevention of further spread.

Methods: We analyzed host adaptability, evolutionary and epidemiological history of MAYV strains collected within the Amazon basin, São Paulo State, and Haiti. Bayesian phylogeography based on molecular clock calibrated genealogies was used to investigate the spatiotemporal spread of MAYV lineages in South American and the Caribbean areas, as well as to infer the origin of detected recombination events.

Results: Our analysis revealed specific adaptations to a broad host and vector range, including humans and the Aedes mosquito species, and assessed recombination events. The first recombinant strain appeared between 2002 and 2013 in Pará State (Brazil), and moved to São Paulo State, giving rise to a second recombinant that was eventually isolated in Haiti in 2015.

Conclusions: We hypothesize that human mobility and adaptability to a broad range of host and vector species played a central role in the emergence of recombinant strains, which are usually rare among arboviruses. Moreover, the potential urbanization of this virus might be the beginning of a much larger, more global epidemic and deserves, therefore, close monitoring in the immediate future.

6. Melissa Vilaro

Department: Food Science & Human Nutrition
College: Agricultural and Life Sciences

Food choice priorities predict fruit and vegetable intake among college freshmen enrolled in the Get Fruved study

Co-Authors: Anne Mathews, Tracey Barnett, Carol Byrd-Bredbenner, Wenjun Zhou, Kristin Riggsbee, Melissa Olfert, Tanya Horacek, Morgan Sowers, Sarah Colby

Abstract:
Background: College freshmen represent a unique group with risk-factors for poor diet and weight gain. This study assessed changes in food choice priorities (FCP) after one year of college and the association between FCP and fruit and vegetable (FV) intake.

Methods: The Food Choice Priorities Survey (FCPS) was developed and validated to assess the importance of various factors for making food choices. Freshmen from eight universities completed the FCPS and the National Cancer Institute's FV screener. Changes in FCPS scores from fall 2015 (baseline; n=1,146) to spring 2016 (follow-up; n= 853) were assessed using paired t-tests. Linear regression analysis examined associations between FCP and FV intake at follow-up.

Results: From baseline to follow-up, the impact of advertising environment, busy lifestyle and preferences, price, stress, and significant others on food choice increased, while the importance of family on food choice decreased ($p<.05$). FCP did significantly predict FV consumption at follow-up. Greater importance placed on factors describing busy lifestyle and preferences (taste, convenience, routine, ability to feel full) (-.24 servings; $p<.05$) and price (-.12 servings; $p<.05$) predicted lower FV intake. When students endorsed health factors as important for food choice (health, effect on physical appearance, freshness/quality/in season), they consumed more FV (+.48 servings; $p<.05$).

Conclusions: Self-rated importance of factors influencing food choice, as measured by the FCPS, is predictive of FV consumption in a university student population. When food choices are driven by price or personal preferences and constrains of a busy lifestyle, students eat fewer FV, signaling potential points of intervention.

Poster Presentations

1. **Brooke A. Armfield**, Molecular Genetics and Microbiology, Medicine
   Loss of the hedgehog pathway prevents separation of the urogenital and anorectal organs.

2. **Tanumoy Bera**, Horticultural Sciences, Agricultural and Life Sciences
   Water footprint analysis of potato production in Northeast Florida

3. **Sunisa Chirakul**, Molecular Genetics and Microbiology, Medicine
   Ceftazidime resistance in Burkholderia pseudomallei in absence of externally acquired resistance determinants

4. **Shreyasi Choudhury**, Ophthalmology, Medicine
   Novel AAV variants isolated by directed evolution in primate display enhanced retinal transduction following intravitreal injection

5. **Samantha Dykes**, Radiation Oncology, Medicine
   Cathepsin L/K inhibition reduces invasion of M2-like macrophages

6. **Maha El Badry**, Environmental and Global Health, Public Health and Health Professions
   Submicroscopic Malaria Infections in Pregnant Women from Six Departments in Haiti

7. **Daniel Ence**, School of Forest Resources and Conservation, Agricultural and Life Sciences
   Genetic Diversity in Candidate Disease-Resistance Genes in Pinus taeda L.

8. **Elizabeth Flood-Grady**, STEM Translational Communication Center & Clinical Translational Science Institute, Journalism and Communications
   The importance of parent-child communication about depression in shaping the health decisions of young adults with depression

9. **Natalie C. Fredette**, Pathology, Immunology and Experimental Medicine, Medicine
   A stem cell tactic to address precision medicine in hypertension

10. **Timothy Hamerly**, Infectious Disease and Pathology, Veterinary Medicine
    Function and mechanisms of O-fucosylation of malaria parasite TSR-domain proteins

11. **Chul Han**, Pathology, Immunology, and Laboratory Medicine, Medicine
    Effect of long-term voluntary exercise on age-related hearing loss

12. **Anna Heffernan**, Physics, Liberal Arts & Sciences
    Gravity: From Newton to Einstein and beyond

13. **Tristan T. Hormel**, Mechanical and Aerospace Engineering, Engineering
    Mucin Production Dynamics: Some Say It's Gross, But It's Snot

14. **Stephan C. Jahn**, Pathology, Medicine
    FLT3 ITD mutations downregulate MLLT3 in acute myeloid leukemia

15. **Aritra Kundu**, Electrical & Computer Engineering, Engineering
    Novel neural interface technology for prosthetic limb

16. **Henry Chun Hin Law**, Infectious Diseases and Pathology, Veterinary Medicine
    Novel approaches towards quantifying the cellular responses of the pathogen in malaria transmission biology

17. **Cory Leonard**, Pathology, Immunology and Laboratory Medicine, Medicine
    Chlamydia pecorum induces NFkB activation and IL-6 secretion

18. **Yin Li**, Family, Community and Health System Science, Nursing
    A Comparison of Care between Nurses and Physicians in U.S. Primary Care System

19. **Hemakumara Mutra**, Pediatric Neurology, Medicine
    Identification of a PYROXD1 mutation in an LGMD cohort from Saudi Arabia

20. **Michael Norris**, Infectious Diseases and Pathology, Veterinary Medicine
    Elucidating the biomolecular interactions of sepsis during the emerging infectious disease melioidosis

21. **Cécile Pereira**, Microbiology and Cell Science, IFAS
    Metabolic pathway extraction from text

22. **Camilly Pestana Pires de Mello**, Medicine, Medicine
    Combination therapy with Interferon-alpha and Ribavirin for the Treatment of Dengue Virus

23. **Ismael M. Rodea-Palomares**, Agricultural and Biological Engineering, IFAS
    Inferring drivers of ecological degradation at large spatial scale in Europe

24. **Jugpreet Singh**, Horticultural Sciences, IFAS
    Merging Genomics and Crop Simulation Models to Predict Complex Phenotypes: A Way Forward to Develop Climate-Resilient Crops

25. **Sonal Singh**, Pharmacotherapy and Translational Research, Pharmacy
    Genome Wide Association Study to Identify Pharmacogenomic Variants Associated with Chlorthalidone Induced Glucose Change in African Americans

26. **Amy L. Skibiel**, Animal Sciences, Agricultural and Life Sciences
    Effects of in-utero heat exposure on mammary microstructure and cellular processes during the first lactation of dairy cows

27. **Natasha Weatherspoon-Griffin**, Environmental & Global Health, Public Health & Health Professions
    Localization and novel secretion of a Shiga toxin produced in recently emerged Shigella flexneri isolates

28. **Xiaojuan Zhang**, Pathology, Immunology and Laboratory Medicine, Medicine
    Novel small molecules for the treatment of alpha-1 antitrypsin deficiency

1. Brooke A. Armfield

Department: Molecular Genetics and Microbiology
College: Medicine

Loss of the hedgehog pathway prevents separation of the urogenital and anorectal organs

Abstract:
Structural birth defects result from abnormal development of the embryonic cloaca, the caudal region of the hindgut that divides to form the lower genitourinary tract ventrally and the anorectal tract dorsally. Although mutations in a few key genes have been found to disrupt cloacal division and epithelial cell type differentiation, little is known about the relationship between dorsoventral patterning of the early cloaca and development of the genitourinary and anorectal organs. We tested the hypothesis that dorsoventral polarity is established in the cloacal epithelium before it divides to form the hindgut and genitourinary tracts. RNAseq analysis of dorsal (future anorectum) and ventral (future genitourinary) cloacal epithelia from the early mouse cloaca identified > 700 genes with differential expression. These results suggest that the genitourinary and anorectal cell type identity may be established before morphogenetic separation of the genitourinary and anorectal sinuses.

We investigated the functional consequences of dorsoventrally polarized gene expression in the early cloaca. We discovered that Indian hedgehog (Ihh) is localized to the dorsal region of the cloaca. To test the role of dorsal expression of Ihh in cloacal development, we removed both Sonic hedgehog (Shh), another member of the hedgehog family, and Ihh from the cloacal epithelium. Whereas loss of Shh alone results in some cloacal division, deletion of dorsally restricted Ihh plus Shh results in no urorectal septum or cloacal division. These results provide the first example of dorsoventrally polarized gene expression in the cloaca regulating the formation of the genitourinary and anorectal organs.

2. Tanumoy Bera

Department: Horticultural Sciences
College: Agricultural and Life Sciences

Water footprint analysis of potato production in Northeast Florida

Co-Authors: Guodong Liu, Lincoln Zotarelli

Abstract:
The amount of fresh water (m3) consumed to produce one ton of potato tubers is known water footprint (WF) of potato production. Northeast Florida (NEF) is the leading spring potato producer in the USA. A study was conducted to calculate the WF of the potato production in NEF. To assess WF of NEF potato production, the green, blue and gray components of the WF were calculated by considering the different volumes of water arising from evaporation, rainfall, irrigation, and fertilizer contamination. Crop evapotranspiration, effective rainfall, and irrigation requirement for twelve years were calculated using CROPWAT 8.0 model with four hypothetically chosen planting dates (January 7th & 22nd and February 7th & 22nd). Nitrogen (N) fertilizer was used as an estimator of gray WF (WFgray). The green WF (WFgreen) and blue WF (WFblue) ranged between 24 to 63 and 17 to 98 m3 t-1, respectively among the planting dates in the years. WFgray was the greatest (50%) contributor to the total WF (WFtotal) of potato production in this region. Earlier planting of potato had lower WFblue ($p<0.001$) as compared to late planting showing importance of efficient irrigation management for this crop. Similarly, later years had higher WFtotal as compared to the initial year which may due to lower productivity of potato in the later years. Thus, the findings of this study permit to assess the fresh water appropriation by NEF potato production industry and emphasize the relevance of efficient field management of agricultural practices including irrigation and fertilization.

3. Sunisa Chirakul

Department: Molecular Genetics and Microbiology
College: Medicine

Ceftazidime resistance in Burkholderia pseudomallei in absence of externally acquired resistance determinants

Co-Authors: Nawarat Somprasong, Sirawit Pagdepanichkit, Michael H. Norris, James F. Shirley, Apichai Tuanyok, and Herbert P. Schweizer

Abstract:
Burkholderia pseudomallei (Bp) causes melioidosis, an emerging infectious disease syndrome endemic in the tropical regions of the world. Ceftazidime (CAZ) antibiotic is effectively used for acute phase melioidosis therapy. Deletion of penicillin binding protein 3 (PBP3), a target of CAZ, has been documented in clinical isolates that failed CAZ therapy. However, the main player in CAZ resistance (CAZR) is a Class A PenA β-lactamase. Mutations that cause PenA over-expression or introduce amino acid substitutions (AAS) in critical regions of the protein cause resistance to CAZ and other β-lactam antibiotics. We showed that the PenA AAS D240G or A172T and the nucleotide G to A transition at the -78 position upstream penA were contribute to CAZR. The β-lactamase inhibitor avibactam (AVI) completely restores CAZ susceptibility (CAZS) in the otherwise CAZR isolates. We identified a CAZR Thai clinical isolate, 5041a, that did not contain any mutations in the penA and its upstream region. Since AVI restored CAZS in this strain, CAZR was likely mediated by a β-lactamase. Whole genome sequencing showed that a 33,000 base pair region of chromosome 2 containing penA is amplified in 5041a and that the CAZR of this strain is likely caused by penA gene amplification. Finally, genetic analysis of a CAZR Australian clinical isolate indicated that CAZR is complex and besides target deletions and mutations affecting PenA involves other genes and proteins. Our studies inform strategies aimed at rescuing the activity of existing antibiotics with anti-B. pseudomallei activity, as well as efficacy evaluation of new β-lactam antibiotics.

4. Shreyasi Choudhury

Department: Ophthalmology
College: Medicine

Novel AAV variants isolated by directed evolution in primate display enhanced retinal transduction following intravitreal injection

Co-Authors: Damien Marsic, James Peterson, Diego Fajardo, Antonette Bennett, Paul Gamlin, Mavis Agbandje-McKenna, Sergei Zolotukhin, Sanford L. Boye, Shannon E. Boye

Abstract:

Background: Directed evolution of AAV capsid libraries has identified variants with enhanced transduction of retina following intravitreal (Ivt) injection. In primate retina, improvements were less substantial. We developed a method to generate sortable retinal cells in primate that enabled identifying AAV variants capable of efficient retinal transduction following Ivt injection. In parallel, the same library was screened in mice. After 3 rounds of selection in mice and 2 in macaque, a subset of the most prevalent variants was characterized. The purpose of this study was to evaluate their transduction profiles in mice by Ivt injection.

Methods: Capsid variants contained a self-complementary AAV genome carrying the truncated CBA promoter driving mCherry (sc-smCBA-mCherry). Transduction was quantified in vitro using ocular cell lines. Vectors were Ivt injected into Nrl-GFP mice and transduction was evaluated 4 weeks later by fundoscopy and FACS. AAV2wt and AAV2(quadY-F+T-V) were included for comparison.

Results: After three rounds of screening in mice, two heavily enriched variants, M3-A and M3-B were chosen for analysis. After two rounds of selection in macaque, the 4 most prevalent variants P2-V1, P2-V2, P2-V3 and P2-V4 were analyzed. Interestingly, P2-V1 is identical to M3-B and P2-V4 is identical to M3-A. All variants displayed substantially improved transduction in vitro compared to AAV2wt. The retinal transduction efficiency of P2-V1, P2-V2 and P2-V3 were improved compared to our most efficient rationally designed capsid, AAV2(quadY-F+T-V).

Conclusion: AAV capsids identified by screening in primate and mouse retina show enhanced transduction efficiencies both in vitro and following Ivt injection.

5. Samantha Dykes

Department: Radiation Oncology
College: Medicine

Cathepsin L/K inhibition reduces invasion of M2-like macrophages

Co-Author: Dietmar Siemann

Abstract:
Cathepsins are proteases that normally contribute to the breakdown of lysosomal contents and the increased secretion of lysosomal proteases is commonly observed in cancer cells. Infiltrating immune cells are also considered a key component of the tumor microenvironment and tumor-associated macrophages are known to facilitate tumor cell invasion. Macrophages stimulated with interleukin-4 exhibit a M2, or pro-tumor phenotype, and show enhanced secretion of cathepsin L compared to unstimulated macrophages. To test the role of cathepsin L in macrophage mediated pro-tumor functions, we utilized novel cathepsin L/K inhibitors KGP94 and KGP207 [Kevin Pinney, Baylor University]. M2 macrophages treated with KGP94 and KGP207 had reduced in vitro invasion toward 4T1 murine breast cancer cell-conditioned media. Interestingly, KGP94 and KGP207 reduced the expression of the M2 marker Arginase-1, suggesting that these inhibitors may prevent the transition from the M0 to M2 phenotype. KGP94 and KGP207 treatment also reduced in vitro invasion of 4T1 cells toward M2 macrophage-conditioned media. These data highlight the relevance of cathepsin secretion from both tumor cells and tumor-associated macrophages and suggest that cathepsin L inhibition is a viable approach for the treatment of tumor associated with macrophage infiltration.

6. Maha El Badry

Department: Environmental and Global Health
College: Public Health and Health Professions

Submicroscopic Malaria Infections in Pregnant Women from Six Departments in Haiti

Co-Authors: Massimiliano S. Tagliamonte , Christian P. Raccurt, Jean F. Lemoine, Alexandre Existe, Jacques Boncy, Thomas A. Weppelman , John B. Dame, Bernard A. Okech

Abstract:

Objectives: Hispaniola is the last island in the Caribbean where malaria transmission remains endemic, with the majority of infections occurring in Haiti. Though pregnant women area high-risk group for malaria infections, surveillance or intervention programs targeting pregnant women in Haiti are rudimentary at best. Thus, data on malaria in pregnancy (MIP) in Haiti are sparse and risk factors for infection have not previously been investigated.

Methods: A cross-sectional study was conducted among pregnant women in six departments of Haiti. Whole blood samples and demographic surveys were collected to investigate malaria prevalence, anemia and socio-behavioral risk factors for infection, respectively. A total of 311 pregnant women were screened for Plasmodium falciparum infection using a rapid diagnostic test (RDT), a microscopy, a novel, quantitative reverse-transcriptase polymerase chain reaction methodology (qRT-PCR).

Results: Overall, 1.2% (4/311) of pregnant women were positive for malaria infection by both microscopy and RDT. However, using the qRT-PCR, 16.4% (51/311) of pregnant women were positive. The prevalence of malaria infection varied with geographic locations ranging between 0% to 46.4%. Additionally, 53% of pregnant women had some form of anemia; however no significant association was found between anemia and submicroscopic malaria infection. The socio-behavioral risk factors identified to be protective for malaria infection were marital status ($P<0.05$) and travel within one month prior to screening ($0<0.05$).

Conclusion: This study is the first to document the high prevalence of submicroscopic malaria infections among pregnant women in Haiti and identify social and behavioral risk factors for disease transmission.

7. Daniel Ence

Department: School of Forest Resources and Conservation
College: Agricultural and Life Sciences

Genetic Diversity in Candidate Disease-Resistance Genes in Pinus taeda L.

Abstract:

Fusiform rust is a disease incited by the fungus Cronartium quercuum f.sp. fusiforme (Cqf) on southern pines (where it causes galls on stems and branches) and on oaks (where it causes minimal leaf damage). Fusiform rust is a major disease threat to the timber industry in the US. Rust galls cause annual yield losses that exceed US$100M. The genome annotation of loblolly pine (Pinus taeda) has become an essential resource for understanding the genetic basis of resistance to fusiform rust disease (Neale et al. 2014 and Wegrzyn et al. 2014). During the genome annotation process, an expressed sequence tag (EST) was identified that contains a single nucleotide polymorphism (SNP) mapping to the locus (Fr1) that interacts with the fungal avirulence gene, Avr1. This EST aligns to a full-length transcript from RNA-sequencing data and a TIR-NB-LRR protein, thus identifying it as a candidate Fr1 gene. In order to understand the population genetic context of this and other pine resistance genes, we sequenced and assembled RNA sequencing data from 92 elite rust-resistant loblolly pine genotypes from five pine-growing regions, identifying candidate resistance genes in the process. Next we aligned the assembled transcripts to the loblolly pine genome and calculated population genetic measures. These results allow us to understand the diversity and conservation of resistance genes that interact with Cqf and in elite genotypes that are important to pine breeding for their fusiform rust resistance and growth traits.

8. Elizabeth Flood-Grady

Department: STEM Translational Communication Center & Clinical Translational Science Institute
College: Journalism & Communications

The importance of parent-child communication about depression in shaping the health decisions of young adults with depression

Abstract:
Young adults (18-25) in the U.S. are among those at greatest risk for developing depression, yet they are the least likely to seek treatment. Because failure to seek treatment places them at an increased risk for alcohol abuse and death by suicide, it is critical to identify factors that influence the health decisions of young adults with depression. One way to understand how young adults develop their attitudes and health decisions surrounding depression is to investigate how their parents communicate with them about these illnesses. Although several sources of socialization are relevant over the life course, parents play a critical role in shaping their children's attitudes and related health decisions through their communication and behaviors.

Young adults (N = 360) who: (1) were between 18-25; (2) had been diagnosed with depression reported on their communication with their parents about depression and on their related health decisions via a survey. The majority of young adults reported communicating with both parents/guardians about depression (n = 230, 69.3%). Parental perspective-taking negatively predicted depression ($p < .001$) and suicidal ideation ($p < .05$); a conversation orientation (i.e., parents who emphasized shared thoughts, feelings, and opinions about depression) positively predicted treatment seeking ($p < .05$) whereas a conformity orientation (i.e., parents who emphasized similarity in views and beliefs often through control) positively predicted binge drinking and suicidal ideation ($p < .01$) among young adults. The results suggest that how parents communicate with their young adult children about depression shapes their children's health and health decisions.

9. Natalie C. Fredette

Department: Pathology, Immunology and Experimental Medicine
College: Medicine

A stem cell tactic to address precision medicine in hypertension

Co-Authors: Katherine Santostefano, Eric R Prossnitz, Julie A Johnson, Naohior Terada

Abstract:
Hypertension (HTN), is a polyfactorial disease that can manifest severe cardiovascular pathologies such as heart failure or stroke. Genome Wide Association Studies (GWAS) of resistant HTN by the UF College of Pharmacy indicate that single nucleotide polymorphisms (SNP) contribute to increased risk for HTN and resistance to some HTN drug regimens. The pharmacogenomics PEAR (Pharmacogenomic Evaluation of Antihypertensive Response) study at the University of Florida has identified multiple SNPs associated with differential drug responses; however, the cellular mechanistic insights of such SNPs remain unknown. We propose to utilize patient-derived induced pluripotent stem cells (iPSC) as a tool to investigate functional changes in vascular cells resulting from SNPs in hypertensive patients. A SNP in the gene for G protein-coupled estrogen receptor (GPER) correlates with increased BP in women. We hypothesize that the GPER SNP changes function in both endothelial cell (EC) nitric oxide dynamics and vascular smooth muscle cell (vSMC) oxidative species balance, resulting in a HTN phenotype. We have completed a gene-editing of the GPER SNP in iPSCs from 3 female HTN patients using CRISPR-cas9, and have differentiated them into EC and vSMC using a dichotomous CD34 sorting protocol. Utilizing this novel resource, we are now investigating functional changes in cellular function in both EC and vSMC to determine the net effect of the GPER SNP in HTN onset. This project is a proof of principle, research endeavor that utilizes iSPCs to bridge clinical studies and GWAS endeavors by providing cellular mechanistic insights.

10. Timothy Hamerly

Department: Infectious Disease and Pathology
College: Veterinary Medicine

Function and mechanisms of O-fucosylation of malaria parasite TSR-domain proteins

Co-Authors: Sílvia Sanz, Rebecca Tweedell, Garima Verma, Timothy Hamerly, Bernadette Hritzo, Abhai Tripathi, Kristina Han, James M. Rini, Matilde de las Rivas, Ramón Hurtado-Guerrero, Rhoel R. Dinglasan, Luis Izquierdo

Abstract:
The thrombospondin type I repeat (TSR) domains of several key proteins of the malaria parasite facilitate attachment to human and mosquito host cells. We hypothesize that the Plasmodium biosynthetic machinery modifies these domains with the sugar fucose, using a protein-O-fucosyltransferase 2 (PoFUT2) enzyme. Throughout the life cycle of Plasmodium, multiple proteins are expressed on the surface of the parasite and contain TSR domains. Our aim is to describe this modification and evaluate its biological significance during the parasite transmission from humans to mosquitoes and back. To test our hypothesis, we have generated a PoFUT2 null mutant of Plasmodium and compared the grow and survival of parasites throughout multiple stages of the life cycle. Furthermore, we have characterized by mass spectrometry one of the most abundant proteins on the sporozoite stage of the parasite, showing that TSR domain of circumsporozoite protein (CSP) is indeed fucosylated by human PoFUT2.

11. Chul Han

Department: Pathology, Immunology, and Laboratory Medicine
College: Medicine

Effect of long-term voluntary exercise on age-related hearing loss

Abstract:

Regular physical exercise reduces the risk for obesity, cardiovascular diseases, and disability, and is associated with longer lifespan expectancy. In contrast, decreased physical function is associated with hearing loss among older adults. Here, we investigated the effects of long-term voluntary wheel running on age-related hearing loss (AHL) in CBA/CaJ mice, a well-established model of AHL. Running activity peaked at 6 months of age (12280 meters/day) and gradually decreased over time. At 24 months of age, the average running distance was 3987 meters/day. Twenty-four-month-old runners had less cochlear hair cell and spiral ganglion neuron (SGN) loss, and had better auditory brainstem response (ABR) thresholds at the low and mid frequencies compared to age-matched non-running controls. Gene Ontology (GO) enrichment analysis of inner ear tissues from 6-month-old controls and runners revealed that wheel running resulted in a marked enrichment for GO gene sets associated with immune response, inflammatory response, vascular function, and apoptosis. In agreement with these results, there was reduced stria vascularis atrophy and reduced loss of capillaries in the stria vascularis of old runners versus old controls. Given that stria vascularis holds numerous capillaries that are essential for transporting oxygen and nutrients into the cochlea, our findings suggest that long-term exercise delays the progression of AHL by reducing age-related loss of strial capillaries associated with inflammation.

12. Anna Heffernan

Department: Physics
College: Liberal Arts & Sciences

Gravity: From Newton to Einstein and beyond

Co-Authors: Ryan Lang, Cliff Will

Abstract:
Our everyday world can be described incredibly with Newtonian mechanics. If one looks to the stars, however, this no longer suffices. There, Einstein's theory of relativity rules; explaining what Newton's could not but also predicting exotic concepts and objects; black holes, objects so compact not even light can escape their gravitational pull; and gravitational waves, ripples in the fabric of space time in which we exist, are two such examples.

With overwhelming success experimentally, and a beautiful reduction to Newton's theory on Earth, Einstein's relativity is our standard model. However, when one looks outside our solar system, there are still unexplained observations. Could there be another theory that reduces to Einstein's in our solar system?

Such theories are commonly known as alternative theories of gravity (ATGs) and have been tested extensively in the weak gravity regime. In 2016, gravitational wave astronomy became a reality. The LIGO/VIRGO collaboration successfully detected gravitational waves emitted from binary black holes. Such detectors can be used to test ATGs in the strong field regime, all we need are waveforms – accurate models of the gravitational waves emitted from binary systems.

One of the longest standing ATGs, scalar-tensor gravity is also one of the simplest; through a varying gravitational "constant". We are currently calculating the waveform for scalar tensor gravity with the post-Newtonian approximation scheme to second order. We have successfully calculated the source term and are working towards the full waveform, which upon calculation will be used to search for deviations from Einstein's theory of relativity.

13. Tristan T. Hormel

Department: Mechanical and Aerospace Engineering
College: Engineering

Mucin Production Dynamics: Some Say It's Gross, But It's Snot

Co-Authors: Tapomoy Bhattacharjee, Angela A. Pitenis, Christopher S. O'Bryan, Juan M. Uruena, W. Gregory Sawyer, Thomas E. Angelini

Abstract:
Mucous layers form at the apical surface of many epithelia, protecting tissues from pathogens and environmental wear and damage. Although these layers contain many materials they are primarily composed of mucin glycoproteins, the concentration of which may be physiologically controlled to maintain specific rheological properties and to provide proper lubrication. Nowhere is this truer than at the surface of the eye's corneal epithelium, where the mucous layer must additionally achieve structural integrity to withstand the stresses created by blinking, and remain transparent in order to enable vision. I will present results on the growth dynamics, concentration, and rheology of a model corneal epithelial mucous layer, all of which can be viewed as important parameters at this interface. I will also discuss modulation of the mucous layer's dynamics with variation in environmental conditions.

14. Stephan C. Jahn

Department: Pathology
College: Medicine

FLT3 ITD mutations downregulate MLLT3 in acute myeloid leukemia

Co-Authors: Matthew Smonskey, Petr Starostik

Abstract:
FMS like tyrosine kinase 3 (FLT3) is one of the most frequently mutated genes in acute myeloid leukemia, with the most common mutation being internal tandem duplications (ITDs). These ITDs lead to FLT3 becoming active through autophosphorylation, and result in changes in signaling pathway activation. Using expression microarrays, RNA-Seq, and qPCR, we have shown that exogenous expression of FLT3-ITD in a leukemic cell line decreases MLLT3 mRNA levels compared to cells expressing FLT3-WT. Since the protein product of MLLT3, AF9, is known to regulate HOX genes through the super elongation complex, this finding is likely important in improving treatment of patients harboring these mutations. We are currently utilizing CRISPR technology followed by RNA-Seq in order to test our proposed mechanism that FLT3-ITD regulates MLLT3 through the activation of ERK.

15. Aritra Kundu

Department: Electrical & Computer Engineering
College: Engineering

Novel neural interface technology for prosthetic limb

Co-Authors: Erin Patrick, Francisco Delgado, Seth Curlin, Ahmed Fahmy, Ryan Madler, Kevin Otto, Nima Maghari, Rizwan Bashirullah

Abstract:
The loss of an upper limb has a profound physiological and psychological effect on the daily life activity of an amputee, as the hand experiences a more direct extension of the brain than any other part of the body (known as a somatosensory homunculus). Currently there are about 105,000 persons with upper limb amputations, with approximately 13,000 new cases every year, in the USA. The dependency of the amputee on others can be reduced if motor and sensory feedback functions can be restored using a state-of-the-art prosthetic arm. This necessitates a novel neural interface capable of generating stimulation patterns that induce realistic sensory percepts with high spatial sensitivity to replicate the missing sensory feedback. The Implantable multimodal peripheral recording and stimulation system (IMPRESS) is a novel technology, consisting of dedicated pair of stimulating and recording integrated-chips coupled with a high-density Transverse Intrafascicular Multichannel Electrode (hd-TIME). In a preliminary study, an hd-TIME was implanted in the sciatic nerve and two recording cuff electrodes were implanted in sural and peroneal nerve branches. Compound action potential electrophysiological data were recorded for a range of stimulus parameters, viz. pulse frequencies, amplitudes and pulse widths, provided by the stimulator chip. An ideal stimulation of nerve fibers to elicit meaningful sensory afferent signals requires understanding and optimizing a wide range of these parameters. We are performing several in vivo experiments to test efficacy of IMPRESS and optimize these stimulation parameters.

16. Henry Chun Hin Law

Department: Infectious Diseases and Pathology
College: Veterinary Medicine

Novel approaches towards quantifying the cellular responses of the pathogen in malaria transmission biology

Co-Authors: Dingyin Tao, Ceereena Ubaida-Mohien, Rhoel R. Dinglasan

Abstract:
As proteomic techniques provide a robust means to identify and quantify proteins globally, they are useful tools to unravel the complex host-pathogen interactions of Plasmodium parasites, the malarial pathogens, and in particular, explore the developmental programming of the transmission stages of the parasite. In the human host, a small portion of the asexual parasite population undergoes sexual development to become gametocytes, a mosquito transmissible form. Using a Systematic Subtractive Bioinformatic analysis on the NF-54 and Dd2 gametocyte proteomic data, we have established a male- and a female-enriched gametocyte proteome. In addition, three female specific genes PF3D7_0906100, PF3D7_0309100, and PF3D7_1218800 were identified as potential female-enriched biomarkers. Even though characterizing the proteome of early sex-specific gametocyte would help to understand mature gametocytes, it has been a daunting analytical challenge to study the initiation of male-female divergence during the immature gametocyte stages, especially for the male gametocytes, due to their smaller size, reduced number (1 male for every 4 females) and a lower overall protein abundance per cell. Clearly, new methods to characterize these earlier male gametocyte developmental stages are needed to overcome this obstacle. We postulate that MS1 intensity based label-free quantification is a suitable LC-MS/MS method to characterize the developing gametocyte proteome because: (1) there is no sample loss due to the chemical labeling process; and (2) this approach provides sufficient sensitivity to capture the potential biomarkers in very limited amount of samples. Combined with the subtraction strategy previously demonstrated, we aim to identify sex-specific biomarkers for the stage I-II gametocytes. In the preliminary experiment, 356 proteins and 1462 peptides were identified after a triplicate analysis for the asexual and gametocyte proteome. Based on the signal intensities, retention time consistency and the identification confidence of individual peptides in the LC-MS/MS analysis, 779 peptides were selected for MS1 intensity based quantification. Transmission-blocking vaccine targets like 6-cysteine protein (PF3D7_0209000), osmiophilic body protein G377 (PF3D7_1250100) and putative secreted ookinete protein (PF3D7_0513700) were identified among the gametocyte enriched proteins. In addition, PF3D7_1430800 and PF3D7_1431100, which were previously found in developing gametocytes (stage I/II), were also found enriched in the gametocyte proteome. These results demonstrate that the quantification approach could provide sufficient sensitivity to identify proteins enriched during gametocytogenesis.

17. Cory Leonard

Department: Pathology, Immunology and Laboratory Medicine
College: Medicine

Chlamydia pecorum induces NFkB activation and IL-6 secretion

Co-Author: Nicole Borel

Abstract:
Background: The pro-inflammatory transcription factor nuclear factor kappa B (NFkB) plays an important role in the host immune response to infection. Epithelial cells release inflammatory cytokines, such as interleukin-6 (IL-6), in response to chlamydial infection, an effect that may be regulated in part by NFkB. The inflammation characteristic of chlamydial infection may be associated with severe disease or contribute to poor overall fitness in farmed animals. We evaluated the ability of porcine chlamydiae to induce NFkB activation and IL-6 secretion in vitro.

Methods: NFkB nuclear translocation, a redistribution of NFkB that occurs in association with activation, was determined by immunofluorescence microscopy. NFkB activation was confirmed by an ELISA-style assay using the NFkB consensus sequence as a target. IL-6 secretion was evaluated by ELISA assay of culture supernatants.

Results: C. pecorum infection induced NFkB nuclear translocation and activation rapidly, by 2 hours post infection (hpi), an effect strongly enhanced by suppression of host de novo protein synthesis. C. suis and C. trachomatis showed reduced capacity for NFkB activation compared to C. pecorum. At 24 hpi, C. pecorum-dependent NFkB activation remained significant and was not abolished by penicillin-induced chlamydial stress. C. pecorum-dependent secretion of IL-6 was also observed at 24 hpi, and this effect, too, was unchanged by penicillin-induced chlamydial stress.

Conclusions: These results suggest that NFkB participates in the early inflammatory response to C. pecorum, and that stressed chlamydiae remain capable of promoting NFkB-mediated inflammation.

18. Yin Li

Department: Family, Community and Health System Science
College: Nursing

A Comparison of Care between Nurses and Physicians in U.S. Primary Care System

Co-Authors: Mark Holmes, PhD; Erin P. Fraher, PhD; Barbara A. Mark, PhD, RN, FAAN; Cheryl B. Jones, PhD, RN, FAAN

Abstract:
Background: Primary care nurses (PCNs) – registered nurses and nurse practitioners – and primary care physicians (PCPs) are being called upon to collaborate and coordinate with each other. Understanding how the care they provide overlaps or is distinct can optimize their utilization in the changing system. The purpose of this study is to examine how nursing care and physician care is similar to and different from each other.

Methods: This cross-sectional study used pooled data from the Household Component of the Medical Expenditure Panel Survey, 2002-2013. Propensity score matching was used to select the study sample, including 2,090 respondents – 1,045 each who saw PCNs or PCPs as a usual source of care (USC). These respondents made 7,821 provider visits, which were analyzed using descriptive statistics and multinomial logistic regression.

Results: PCNs were more likely to provide therapeutic or preventive care, while PCPs were more likely to provide diagnostic care and biomedical treatment. PCNs and PCPs managed similar diagnoses when serving a usual provider role. When PCNs served a supplemental role, they were more likely to manage patients with a diagnosis of the genitourinary system or neoplasm. When PCPs served a supplemental role, they were more likely to manage patients having a diagnosis of the circulatory or musculoskeletal systems, or an injury or poisoning.

Conclusions: Managers of primary care practices and healthcare systems may adjust organizational policies and allow PCNs and PCPs to deliver services/therapies that best utilize their expertise. PCNs may be encouraged to serve as a usual provider for patients.

19. Hemakumara Mutra

Department: Pediatric Neurology
College: Medicine

Identification of a PYROXD1 mutation in an LGMD cohort from Saudi Arabia

Co-Authors: Reddy, Hemakumar M; Salih, Mustafa A; Jones, Michael D; Mitsuhashi, Satomi; Cho, Kyung-Ah; Estrella,Elicia; Lek, Monkol; Valkanas, Elise, Kunkel, Louis M; MacArthur, Daniel G; Kang, Peter B

Abstract:
Abstract:
Limb-girdle muscular dystrophy (LGMD) is a neuromuscular disorder characterized by progressive proximal muscle weakness, accompanied by classic histological findings on muscle biopsy. A large number of genes have been associated with different types of LGMD. We have recruited and analyzed 18 additional families with LGMD from Saudi Arabia after our previously published study. One or more individuals demonstrating the LGMD phenotype from each family were analyzed along with unaffected individuals from those families.

Initial analysis was performed to identify mutations in known genes using traditional approaches including immunohistochemistry and Sanger sequencing. For 7 families who remained undiagnosed after the initial analysis, exome sequencing was performed on probands, along with available parental samples. Candidate mutations in known LGMD genes were identified in the exome data and confirmed via Sanger sequencing. Co-segregation with the phenotype was confirmed in all informative DNA samples.

Of the 16 families analyzed, 8 were found to have pathogenic mutations in known muscle disease genes, primarily LGMD genes. One family was found to have a mutation in PYROXD1, a gene that only recently has been associated with LGMD.

In conclusion, this study identified causal mutations in ~50% of LGMD families in this cohort from Saudi Arabia. In particular, exome sequencing identified a pathogenic PYROXD1 mutation that was recently reported in families of Turkish and Persian Jewish origin.

20. Michael Norris

Department: Infectious Diseases and Pathology
College: Veterinary Medicine

Elucidating the biomolecular interactions of sepsis during the emerging infectious disease melioidosis

Co-Authors: Herbert Schweizer, Apichai Tuanyok

Abstract:
Background: The emerging tropical disease melioidosis is a severe emerging tropical disease with a high mortality rate. The major cause of death is complications from septicemia, which is triggered by the immune response to lipopolysaccharide (LPS) components of the Gram-negative bacterial membrane of Burkholderia pseudomallei (Bp).

Methods: Time-lapse fluorescent live-cell microscopy was used to observe multinucleated giant cell formation during cell infection. MALDI-TOF was used to analyze the mass of lipidA in response to bacterial growth at human body temperature. Effects on binding to human septic response protein LBP were investigated via surface plasmon resonance. Variable ability of LPS to induce immune genes in mouse macrophage and human PBMCs was investigated by innate and adaptive immunity qPCR arrays. MAGPIX multiplex cytokine 10-plex panel was used to measure cytokine secretion by human PBMCs responding to LPS treatment.

Results: Bp strains change its lipidA structure in response to growth at body temperature, resulting in weaker binding to hLBP. The structures also result in weaker innate immune gene induction and cytokine secretion.

Conclusions: These findings add to the evolving knowledge of host-response to bacterial LPS and can be used to better understand sepsis in melioidosis patients. Understanding the mechanisms by which a variety of Bp strains or serotypes cause septic shock can reduce mortality associated with melioidosis but also allow for rational design of effective vaccines. As we investigate further, the intricacies of Bp infection become more complex, increasing the depth and breadth of our understanding of bacterial immunopathogenesis.

21. Cécile Pereira

Department: Microbiology and Cell Science
College: IFAS

Metabolic pathway extraction from text

Co-Author: Ana Conesa

Abstract:
Background: The metabolism is defined as the chemical processes that occur within a living organism in order to maintain life. It exists, at least 35 databases listing metabolic pathways [1]. These databases differ by the organisms and processes represented. It was shown that even for the same organism, the recovery between these databases is smaller than 16% [2]. Thus, how to recover a complete pathway?
Methods: We propose to automatically extract metabolic and signaling reactions involved in a list of processes given by the user. Our method combines abstract selection methods with text mining, databases of metabolic reactions, and ortholog detection methods to provide a complete and accurate set of compounds, genes and reactions.
Results: We tested the methodology on two well described pathways in plants and bacteria. We show that this methodology allows to recover more than 90% of the genes and compounds described in metacyc [9]. Moreover, even for these well known pathways, it proposes new entities and reactions possibly involved in the process and actually described in the literature.
Conclusions: This pipeline allows to recover information coming from hundred of abstracts into a single pathway describing a process of interest.

[1] Metabolomics Society: http://metabolomicssociety.org/resources/metabolomics-databases.
[2] Stobbe, M. et al. BMC Systems Biology 5, 165 (2011).
[3] Caspi, R. et al. Nucleic Acids Research 38, (2009).

22. Camilly Pestana Pires de Mello

Department: Medicine
College: Medicine

Combination therapy with Interferon-alpha and Ribavirin for the Treatment of Dengue Virus

Co-Authors: G.L. Drusano, J.J. Pomeroy, E.J. Franco, J.L. Rodriquez, A.N. Brown

Abstract:
Dengue virus (DENV) is the most prevalent mosquito-borne human viral disease. There are no therapeutic agents available to prevent or treat DENV infections. Our objective was to fill this unmet medical need by evaluating the antiviral activity of interferon-α (IFN) and ribavirin (RBV) as combination therapy against DENV. Vero and Huh-7 cells were infected with DENV in the presence of increasing concentrations of IFN and/or RBV. Supernatants were harvested and viral burden was quantified by plaque assay on Vero cells. A mathematical model was fit to the data to define drug-drug interactions for antiviral effect. In Vero cells, the effect of IFN and RBV was additive with EC50 values of 1,222 IU/ml and 100.7 mg/L, respectively. Drug interactions were highly synergistic in Huh-7 cells, yielding EC50 values of 72.24 IU/ml for IFN and 46.58 mg/L for RBV. The antiviral activity of the IFN plus RBV at clinical exposures was also evaluated in an in vitro plate assay. Clinically-relevant exposures inhibited DENV by 2-log10 at 24h and 48h post-treatment in Vero cells. Inhibition was much higher in Huh-7 cells, as viral burden was suppressed by 3.3-log10 at 24h and 4.6-log10 at 48h. Host cell selection is important for antiviral screening assays, as different cell lines may result in different conclusions. Since Huh-7 is a human hepatocyte cell line it is a more relevant tissue culture model for DENV infection compared to Vero cells. Overall, our results suggest that IFN plus RBV is a potential therapeutic strategy for the treatment of DENV.

23. Ismael M. Rodea-Palomares

Department: Agricultural and Biological Engineering
College: IFAS

Inferring drivers of ecological degradation at large spatial scale in Europe

Co-Authors: Rafael Muñoz-Carpena; Nikolay Blyzniuk, Hunter R. Merril

Abstract:
During the last decades, Ecotoxicology has drawn the basic “cartography” of chemical pollution and its potential ecological impacts. However, these maps are still fragmented and not ready to answer apparently simple questions from the real world such as: what is the main driver on the observed ecological alterations at a certain scale?; is it organic chemical pollution or other factor such as just nutrient enrichment or hydrological alteration?; in a common scale metric, which of these factors are more important? Few studies addressed large-scale ecological effects of chemical pollution, and even fewer are examine the relative contribution of organic chemical pollution in the context of other relevant chemical or non-chemical factors. Data scarcity, data fragmentation, and the unavailability of chemical pollution remote sensing data hampers such large scale integrated studies. The present talk will cover the aims, methods and preliminary results of a project that aims to infer large-scale patterns of ecological degradation that can be assigned to chemical pollutants in the context of other potential stressors. This will be addressed with a novel integration of data mining, statistical machine learning and spatially distributed Global Sensitivity and Uncertainty Analysis (GSA/UA). The project mines data from the largest database of chemical pollution in Europe made available by the European Commission: more that 16000 monitoring stations, with more than 560 monitored chemical pollutants under screening. The ultimate aim is to build relative importance map for different chemical pollutants in the context of other ecological stressors at the continental scale (Europe).

24. Jugpreet Singh

Department: Horticultural Sciences
College: IFAS

Merging Genomics and Crop Simulation Models to Predict Complex Phenotypes: A Way Forward to Develop Climate-Resilient Crops

Co-Authors: Jugpreet Singh, Mehul Bhakta, Melanie J. Correll, Christopher Hwang, Salvador Gezan, Pepe Clavijo Michelangeli, James W. Jones, Kenneth J. Boote, Eduardo C. Vallejos

Abstract:
Climate change is causing drastic crop yield losses worldwide. Combining tools for genome analysis with those provided by crop simulation models (CSMs) can produce gene-based models to simulate crop performance under defined environmental conditions, including about the ones by climate change. Currently, dynamic CSMs can capture site-specific information and predict the adaptability potential of crop germplasm to specific environments. These models require two types of input: environmental data comprising soil characteristics, weather, and management practices throughout the growing season, and quantitative intrinsic characteristics of genotypes in a particular crop. The latter are obtained by calibrating the model with each genotype to generate a set of genotype-specific model parameters using complex statistic methodologies. We attempted to extract the genetic information from model parameters using data from a large segregating population grown in a multi environment experiment, but very little genetic information was obtained. It means that the CSM was not constructed with genetics in mind, and that models were optimized to generate parameter values for best predictive ability, regardless of the genetic mechanisms involved. We are now using statistical mixed effects models to capture the genetic, environmental, and genotype-by-environment interaction components of variation to predict the phenotype with almost the same degree of accuracy as the crop simulation model. We are also developing modular crop-growth model, where each module represents a physiological function dictated by the genotype, the environment and their interactions. The new generation of gene-based models could help plant breeders select in silico genotypes adapted to specific environments.

25. Sonal Singh

Department: Pharmacotherapy and Translational Research
College: Pharmacy

Genome Wide Association Study to Identify Pharmacogenomic Variants Associated with Chlorthalidone Induced Glucose Change in African Americans

Co-Authors: Yan Gong, Caitrin McDonough, Rhonda M. Cooper-DeHoff1, Julie A. Johnson

Abstract:
Background: Thiazide and thiazide like diuretics are first line drugs for treating uncomplicated hypertension. However, their use, especially chlorthalidone can be plagued with adverse metabolic events such as hyperglycemia and new onset diabetes, for which the exact mechanism is unknown. We aimed to identify pharmacogenomic variants associated with chlorthalidone induced glucose change.

Methods: Genome-wide association analysis (GWAS) of glucose change post chlorthalidone treatment was performed in 135 African American (AA) patients from the Pharmacogenomic Evaluation of Antihypertensive Responses-2 (PEAR-2) study using linear regression in ProbABEL, adjusting for age, sex, baseline glucose and ancestry. Polymorphisms (SNPs) with $p< 5 \times 10\text{-}8$ were tested for replication in an independent sample of 142 AA treated with hydrochlorothiazide from the PEAR-1 study. A meta-analysis of the two studies was then performed in METAL.

Results: An intronic SNP (rs9943291) in the HMGCS2 gene was associated with increased glucose change post chlorthalidone treatment (ß=12.5, p=4.17X10-8) and replicated in PEAR-1 (ß=5.54, p=0.046), with a meta-analysis p value of 3.71X10-8. HMGCS2, a part of the HMG-CoA synthase family is important for ketogenesis and cholesterol synthesis pathways that are essential in glucose homeostasis. Also, rs9943291 is an eQTL for the PHGDH gene in whole blood. PHGDH gene variants were reported to be associated with increased serine levels and insulin sensitivity.

Conclusion: These results suggest that HMGCS2 and PHGDH are promising candidate genes involved in thiazide induced glucose change and may provide insights into the mechanisms involved in thiazide-induced hyperglycemia that may ultimately facilitate personalized approaches to hypertension treatment.

26. Amy L. Skibiel

Department: Animal Sciences
College: Agricultural and Life Sciences

Effects of in-utero heat exposure on mammary microstructure and cellular processes during the first lactation of dairy cows

Co-Authors: T. F. F. Fabris, C. Meijia, G. E. Dahl, J. Laporta

Abstract:
Intrauterine exposure to high temperatures impacts the developing calf; impairing immune function and reducing milk production during the first lactation. Direct exposure of mature cows to high temperatures alters cellular processes, such as apoptosis (programmed cell death) and proliferation, involved in mammary development, yet it is unclear if in-utero exposure to heat induces similar changes in the mammary gland (MG) of heifers (female calves). Our objective was to determine if cellular processes and mammary microstructure were altered in in-utero heat stressed heifers. Heifers were born to dams housed in barns with fans and soakers (cooled, CL; n = 4) or without cooling devices (heat stressed, HT; n=3) during late gestation. Heifer MG were biopsied at 21 and 42 days in milk (DIM). Tissues were fixed, paraffin embedded, sectioned, and stained with hematoxylin & eosin. The number of alveoli was counted and alveoli area was measured. Immunohistochemistry assays were used to visualize cells undergoing apoptosis and proliferation (i.e. positive cells). The proportion of positive cells to total cells was statistically analyzed. CL and HT heifers had similar alveoli number but area was smaller for HT relative to CL heifers (62,145 vs. 99,088 ± 6,912 µm2; P=0.01). The proportion of cells undergoing apoptosis and proliferation was similar between treatment groups. In contrast to the effects of heat stress on mature cows, indirect exposure to heat during fetal development does not appear to influence cell turnover in the MG of offspring, yet, it alters MG microstructure which may affect lactation performance.

27. Natasha Weatherspoon-Griffin

Department: Environmental & Global Health
College: Public Health & Health Professions

Localization and novel secretion of a Shiga toxin produced in recently emerged Shigella flexneri isolates

Co-Author: Anthony T. Maurelli

Abstract:
The emergence of Shiga toxin (Stx) production by traditionally non-toxin producing Shigella flexneri isolates is cause for concern because Stx is associated with bloody diarrhea and hemolytic uremic syndrome (HUS), a severe and life-threatening kidney damaging sequela. HUS is more commonly associated with infections by bacteria that produce Stx2, which, like Stx, is an RNA N-glycosidase that inhibits protein synthesis and ultimately results in host cell death. Our lab has reported the presence and expression of Stx in S. flexneri clinical isolates. Stx is antigenically distinct but enzymatically identical to Stx2 and is encoded by genes carried by a bacteriophage, φPOC-J13. Here, we demonstrate that Stx from φPOC-J13 is: (i) localized in the periplasm of S. flexneri, (ii) produced independently of bacteriophage-encoded products, and (iii) unlike other Shiga toxins, is released into the extracellular environment independent of phage induction. We hypothesize that a chromosomally encoded, uncharacterized secretion system is responsible for Stx release. A genetic screen using a stx-phoA reporter to identify this novel system is proposed and discussed.

28. Xiaojuan Zhang

Department: Pathology, Immunology and Laboratory Medicine
College: Medicine

Novel small molecules for the treatment of alpha-1 antitrypsin deficiency

Co-Authors: Kien Pham, Susana Restrepo, Austin Bracey, Danmeng Li, Chen Liu, David Ostrov

Abstract:

Introduction: Alpha-1 antitrypsin (AAT) is a glycoprotein primarily synthesized in the liver and secreted into the serum to inhibit neutrophil proteases released during inflammation. AAT deficiency (AATD) is a hereditary disorder related to chronic lung and liver diseases, such as COPD, liver cirrhosis and liver cancer. The Z variant is the most frequent mutation associated with liver diseases. In this phenotype, the protein product of the mutant Z gene misfolded as polymers and cannot be efficiently secreted by the liver. The accumulation of variant AAT as polymers in hepatocytes results in hepatitis, cirrhosis and hepatocellular carcinoma. Currently, liver transplantation is the only curative treatment available for the end-stage liver diseases. Thus, it is essential to develop effective strategies to block polymerization to treat AATD associated disease. Crystal structure analysis has located the critical site that is responsible for polymer formation. The intermolecular interaction site is an attractive target for rational structure-based drug design. In the current study, we aim to identify small molecular compounds active in interfering with AAT polymerization to develop pharmacological therapy for AATD and associated diseases.

Methods: 139,735 compounds, available through the National Cancer Center Developmental Therapeutics Program, were screened by molecular docking using DOCK 5.1 (UCSF) on the UF High Performance Computing Center by parallel processing. Small molecules with top scores (overall energy scores) were used as lead compounds in functional studies to test activity. A human Z-AAT liver cell line was established from transgenic mice expressing human Z variant AAT in the liver. The transgene construct contains the entire human alpha1-antitrypsin (AAT or SERPINA1) gene encoding the Z variant allele which has a Glu->Lys substitution at position. Lead compounds with variant concentrations were tested in human Z-AAT liver cell line. ELISA was used to detect the extracelluar and intracelluar Z-AAT levels. Cell toxicity was measured to exclude the toxic compounds in vitro.

Results: Ten lead compounds with top scores were selected. Three of them have positive effects on decreasing intracellular Z-AAT in human Z-AAT liver cell line. Their structural analogues were identified and tested in vitro. 5-methyl-3-[(6-nitro-2H-1,3-benzodioxol-5-yl)methylidene]oxolan-2-one was screened to have better efficacy and less toxicity.

Conclusions: 1. Active small molecules can be identified by molecular docking based on the AAT crystal structure and functional testing. 2. Small molecules targeting at interfering AAT polymerization is a promising strategy for developing pharmacological therapy for AATD and associated diseases such as liver cancer, COPD and emphysema.