Indiana Clinical and Translational Sciences Institute

ANNUAL MEETING

SCIENTIFIC SESSION ABSTRACTS

VOLUME 10: 2020

AND

RESEARCH CORE/CENTER INFORMATION



Table of Contents

Alphabetic List of Presenters	Page 3
Cell Biology and Biochemistry	<u>Page 5</u>
COVID -19	Page 9
COVID-19 & Immunology	<u>Page 13</u>
Health Implementation I	<u>Page 17</u>
Health Implementation II	<u>Page 21</u>
Microbiology & Immunology	<u>Page 25</u>
Modeling	<u>Page 29</u>
Neuroscience I	<u>Page 33</u>
Neuroscience II	<u>Page 37</u>
Oncology	<u>Page 41</u>
Research Rally Cores/Centers	Page 45

List of Presenters Alphabetical Order

Abebe, Ephrem	Page 30
Alonso, Jesus	Page 14
Alves, Nathan	<u>Page 10</u>
Aruldhas, Blessed Winston	<u>Page 30</u>
Battina, Hanisha	Page 6
Bushey, Michael	<u>Page 38</u>
Camara, Ali	<u>Page 34</u>
Campbell, Angela	<u>Page 18</u>
Chen, Andy	Page 6
Chimelisii-Santiago, Jose	<u>Page 34</u>
Cohee, Andrea	<u>Page 18</u>
Corman, Hannah	<u>Page 26</u>
Couetil, Justin	<u>Page 35</u>
Dir, Allyson	<u>Page 19</u>
Duncan, Francesca	<u>Page 19</u>
Fine, Kimberly	Page 38
Hayes, Lisa	<u>Page 20</u>
Hill, Jordan	<u>Page 10</u>
Huang, Christina	<u>Page 42</u>
Ismail, Heba	<u>Page 26</u>
Janosevic, Danielle	Page 7
Kasting, Monica	<u>Page 22</u>
Kelker, Heather	<u>Page 10</u>
Keller, Grant	<u>Page 14</u>
Kiefer, Brianna	<u>Page 11</u>
Kokoska, Ryan	<u>Page 35</u>
Kumar, Nimisha	<u>Page 22</u>
Lazarus, Jake	<u>Page 15</u>
Libring, Sarah	Page 42
Lindroth, Heidi	Page 15
Lipp, Sarah	Page 7
Liu, Xiao	Page 27
Mapder, Tarunendu	<u>Page 16</u>
Maratt, Jennifer	Page 23
Mathew, Deepa	Page 39
Mesmar, Fahmi	Page 8
Panoch, Janet	Page 23
Patel, Jheel	Page 39

List of Presenters Alphabetical Order (Continued)

Rogers, Edmond	<u>Page 36</u>
Romano, Daniel	<u>Page 40</u>
Sarkar, Kaustabh	<u>Page 43</u>
Savoy, April	<u>Page 31</u>
Sivasubramaniam, Badhu	Page 27
Snapp, Cameron	Page 12
Sohutskay, David	<u>Page 31</u>
Stokes, Michael	Page 32
Van der Jeught, Kevin	Page 43
Viswanath, Dhushyanth	Page 44
Weathered, Catherine	Page 28
Williams, Ebony	Page 24

CELL BIOLOGY & BIOCHEMISTRY

Title: Impacts of Type II Diabetes and BMP-2 in Lung Endothelial Cells for Fracture Healing **Presenter:** Battina, Hanisha

Authors: Hanisha L. Battina, Fazal Ur Rehman Bhatti, Ushashi C. Dadwal, Olatundun D. Awosanya, Seungyup Sun, Caio de Andrade Staut, Stephen K. Mendenhall, Anthony J. Perugini III, Conner R. Valuch, Nikhil P. Tewari, Rohit U. Nagaraj, Rachel J. Blosser, Carmella Evans-Molina, Jiliang Li, and Melissa A. Kacena

Abstract: Type 2 diabetes (T2D) induces various physiological changes in the bone, increasing the risk for fractures. Fracture healing is impaired due to disruptions in angiogenesis and bone formation. Critical-sized bone defects (CSDs) are large, non-union defects that do not heal spontaneously throughout the lifespan of an organism. The lack of blood flow at the site of the CSD requires the intervention of treatments that prompt osteogenesis and re-vascularization. Currently, the only FDA-approved standard that may be used as a bone graft substitute for treating CSDs is bone morphogenetic protein-2 (BMP-2).

Here we examined angiogenic properties of endothelial cells isolated from mice with the T2D phenotype treated with or without BMP-2. The baseline parameters utilized for this study included insulin tolerance test (ITT), glucose tolerance test (GTT), and weekly body weight measurements. The T2D-like metabolic phenotype was induced in mice by placing them on a high fat diet (HFD) while the control mice received a low-fat diet (LFD). Both groups of mice underwent a CSD surgery on their right femur and were treated with either saline (negative control) or BMP-2 (positive control). The effects of BMP-2 on proliferation, vessel formation, and gene expression of endothelial cells were investigated.

2

Title: High-throughput Reporter Assay Reveals Functional Impact of 3'-UTR SNPs Associated with Neurological and Psychiatric Disorders

Presenter: Chen, Andy

Authors: Andy B. Chen1, Kriti Thapa2, Hongyu Gao1, Jill L. Reiter1, Junjie Zhang1, Xiaoling Xuei1, Hongmei Gu2, Yue Wang1, Howard J. Edenberg1,2, Yunlong Liu1* 1Department of Medical and Molecular Genetics, 2Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, Indianapolis, Indiana, United States of America

Abstract: Genome-wide association studies (GWAS) can identify noncoding variants associated with specific traits or phenotypes but cannot distinguish whether such variants are functional. High-throughput reporter (HTR) assays can be used to experimentally evaluate the impact of genetic variants on gene expression. In this study, our objective was to systematically evaluate the functional activity of 3'-UTR SNPs associated with neurological disorders. We gathered SNPs from the GWAS Catalog that were associated with any neurological disorder trait with p-value < 10-5. For each SNP, we identified the region that was in linkage disequilibrium (r2 > 0.8) and retrieved all the common 3'-UTR SNPs (allele-frequency > 0.05) within that region. We further used an HTR assay to measure the impact of the 3'-UTR variants in SH-SY5Y neuroblastoma cells and a microglial cell line. Of the 13,515 3'-UTR SNPs tested, 400 and 657 significantly impacted gene expression in SH-SY5Y and microglia, respectively. These results were then used to train a deep-learning model to predict the impact of variants and identify features that contribute to the predictions. In conclusion, this

study demonstrates that HTR assays combined with advanced machine-learning models can be used to identify causal non-coding variants to further understand the etiology of diseases.

#3

Title: Proximal Tubular S3 Cells Expressing Angiotensinogen Localize to the Outer Stripe of the Outer Medulla

Presenter: Janosevic, Danielle **Authors:** Danielle Janosevic, D.O., KL2 Scholar

Abstract: The S3 segments of proximal tubules (PT) are observed in the cortex and outer stripe of the outer medulla (OS-OM). Using single cell RNA sequencing (scRNAseq), we and others have identified a unique S3 population, referred to as S3-Type 2 (S3T2, Figure a). S3T2 cells uniquely express Rnf24 and Slc22a7, in addition to other S3 markers. We combined spatial transcriptomics (SpT) and scRNAseq to localize this novel S3T2 cell population in the murine kidney. SpT was performed on OCT frozen murine kidney sections and images collected with Keyence microscope. RNA was isolated from tissue, sequenced, and clustering performed. To increase resolution, we combined scRNAseq data with SpT.

Combining scRNAseq with SpT increased spatial resolution from 7 clusters to 15 unique cell clusters on the tissue section. While regular S3 cells localized to the cortex, S3T2 cells localized specifically to the OS-OM (Fig. b). In addition to Rnf24 and Slc22a7, S3T2 cells showed strong expression of angiotensinogen (Agt, Fig. c), possibly indicating a role in the renin-angiotensin system. smFISH of Agt and Aqp1 confirmed these results (Fig. d).

Combining scRNAseq and SpT affords greater resolution in the spatial layout of renal cell populations and provides novel insights into understanding cellular microenvironments.

#4

Title: Elastin-microfibril axis proteins form transient 3D structures during murine nephrogenesis **Presenter:** Lipp, Sarah

Authors: Sarah N. Lipp1,2; Andrew L. Schwarderer3; David S. Hains3; Sarah Calve4; 1Weldon School of Biomedical Engineering, Purdue University, 206 South Martin Jischke Drive, West Lafayette, IN 47907; 2The Indiana University Medical Scientist/Engineer Training Program; 3Indiana University School of Medicine, Riley Children's Hospital, 699 Riley Hospital Dr, Indianapolis, IN 46202; 4Department of Mechanical Engineering, University of Colorado - Boulder, 1111 Engineering Dr, Boulder, CO 80309

Abstract: <u>Background:</u> Dynamic changes in the composition and structure of the extracellular matrix (ECM) are understudied but critical during renal development. Our recent proteomic study indicated proteins in the elastin-microfibril axis were upregulated with development; however, structural changes during maturation are unclear.

<u>Methods</u>: Kidneys were decellularized, stained for elastin-microfibril axis protein (EMILIN1), FREM2, and proteoglycans (WGA), imaged using confocal microscopy, and rendered in 3D using FIJI. <u>Results</u>: At perinatal timepoints, elastin-microfibril axis proteins were organized in the interstitium surrounding developing tubular and glomerular elements, including vertical fibers connecting to the capsule and medullary ray sheath fibers. Patterning was lost in the adult.

<u>Conclusion</u>: The 3D corticomedullary junction structures for elastin-microfibril axis proteins at the perinatal timepoint were consistent with the proteomic trends. We hypothesize the structures are important for nephrogenesis through mechanical support and growth factor modulation.

Title: Adipocyte differentiation and/or lipid accumulation are induced by commonly used pesticides in Indiana

Presenter: Mesmar, Fahmi

Authors: Fahmi Mesmar, Jason Tennessen, Ken Mackie, Stephen J. Carter and Maria Bondesson Indiana University, Bloomington

Abstract: Obesity and obesity-related disorders remain a threat to personal and public health - a trend that is apparent in Indiana wherein nearly 34% of rural residents are obese and symptomatic of related cardio-metabolic disorders. Factors related to excessive fat accretion are multidimensional including genetics, caloric intake, and physical inactivity, however; mounting evidence suggests environmental factors, such as exposure to chemical pollutants, can also contribute to obesity-related diseases. Here, we sought to investigate whether commonly used agricultural pesticides used on corn and soy fields can enhance adipocyte differentiation and lipid droplet formation in vitro. We treated the mouse 3T3-L1 cell line with increasing concentrations of atrazine, flumetsulam, acetochlor, metolachlor, dicamba, tefluthrin, or glyphosate followed by staining for lipids. Of these chemicals, exposure to acetochlor, metolachlor, tefluthrin and atrazine increased lipid staining. Through qPCR we determined that these four chemicals also increased the expression of Fabp4, PPARg, and Lpl, which are markers for pre-adipocytes (early differentiation), adipocyte differentiation and mature adipocytes, respectively. Future studies will determine if these and other chemicals will affect lipid regulation in flies, fish and mice, with the long-term goal of providing the Indiana rural community with information on how to best avoid exposure to obesogenic chemicals.

COVID-19

Title: Real-World Implementation of UV N95 Mask Decontamination in the Hospital Setting **Presenter:** Alves, Nathan

Authors: Nathan Alves, PhD, Indiana University School of Medicine

Abstract: Since the onset of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2 or COVID-19) in December of 2019 there has been >4.6 million infected and >155,000 associated deaths in the US alone. The rapidly evolving healthcare crisis resulting from hospital systems exceeding capacity in addition to limited access to the necessary personal protective equipment (PPE) created unique challenges. Hospital networks took drastic steps to protect frontline providers and patients and mitigate PPE shortages by leveraging systems for decontaminating and reusing what once were considered to be single use disposable items. Of critical importance, are N95 surgical masks that are rated to filter >95% of 0.3 μ m particles and were used heavily in the early phases of the pandemic and have since been restricted for use only during aerosol generating procedures. This poster will focus on the implementation and validation of an ultraviolet germicidal irradiation (UVGI, 254nm) system used to decontaminate N95 masks for the downtown IU Health hospital system. Details regarding the design and building of a PVC mask holding rack (9' wide X 6' tall), placement of UVGI Surfacide tower emitters, UV field intensity mapping (colorimetric and UVC radiometers), and MRSA contaminated mask kill testing will all be discussed.

7

Title: Remotely Delivering a Medication Safety Intervention during a Global Pandemic **Presenter:** Hill, Jordan

Authors: Jordan Hill, Indiana University School of Medicine; Addison Harrington, Regenstrief Institute; Philip Adeoye, Regenstrief Institute; Noll Campbell, Purdue University, College of Pharmacy, Indiana University, School of Medicine, Regenstrief Institute; Richard Holden, Indiana University, School of Medicine, Regenstrief Institute

Abstract: With COVID-19 requiring the suspension of face-to-face research activities, researchers are faced with new obstacles to the continuation of their studies. In order to overcome these research challenges, our team assessed the needs of our study population (older adults) and took an iterative, Agile-inspired approach to developing and testing operational solutions.

#8

Title: Longitudinal Emergency Medicine Provider Burnout and Wellness During the COVID-19 Pandemic

Presenter: Kelker, Heather

Authors: Heather Kelker, MD; Kyle Yoder, MD; Paul Musey, MD; Madison Harris; Olivia Johnson; Brooke Henderson, MD; Punit Vyas; Elisa Sarmiento MS; Zachary Adams, PhD; Julie Welch, MD

Abstract: Importance: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) aka COVID-19 pandemic has had far-reaching consequences to society globally, affecting nearly every aspect of daily life. There is a paucity of research exploring emergency medicine (EM) and non-physician practitioner (NPP) burnout and well-being during a global pandemic.

Objective: The objective of the study is to assess the demographic characteristics, wellness, burnout, resilience, and ongoing needs of EM physicians and non-physician practitioners the frontlines of the COVID-19 pandemic.

<u>Design</u>: Longitudinal prospective cohort survey study.

<u>Setting:</u> Ten academic and community emergency departments across the state of Indiana. <u>Participants:</u> EM physicians and NPPs within the department of EM at Indiana University School of Medicine.

<u>Main Outcomes and Measures</u>: A 41-item questionnaire that was comprised of multiple choice, scaled rating and yes-no questions; and included several validated tools for assessing physician wellness (Well-Being Index), burnout (Physician Work Life Balance single burnout question), and resilience (Brief Resilience Scale).

<u>Results:</u> Concern for personal safety decreased from 85% (96/113) to 61% (40/65, p<0.001). Impacts on basic self-care declined from 66% (75/113) to 32% (21/65; p<0.001). Self-reported symptoms of stress, anxiety or fear was initially at 83% (94/113) but reduced to 66% (43/65; p=0.009) by the end of the study period. Additional work responsibilities steadily declined from 59% (67/113) to 34% (22/65; p=0.001). Reported strain on relationships and feelings of isolation affected more than half of survey respondents initially without significant change over the course of the study period. Physician wellness scores improved over the four-week period, but burnout symptoms did not significantly change.

<u>Conclusions and Relevance</u>: This survey of EM providers found that despite being a resilient group, the majority of frontline EM providers experienced stress, anxiety, fear, and concerns about personal safety due to COVID-19, with many at risk for burnout. The formation of a wellness taskforce, whose objective was to evaluate wellness and elicit actionable items during the early stages of the pandemic, may have contributed to the increases in reported wellness scores and may be a key strategy to improve provider well-being.

9

Title: Obtaining Objective Clinical Measures in Tele-Evaluations of Dysarthria **Presenter:** Kiefer, Brianna

Authors: Brianna Kiefer, MS; Jordanna Sevitz, MS CCC-SLP, Jessica Huber, PhD; Michelle Troche, PhD

Abstract: The COVID-19 pandemic has required speech-language pathologists to utilize telehealth as a primary service delivery method despite there being minimal evidence on how to evaluate patients with motor speech disorders accurately and efficiently via telehealth. In the current study, we provide a tutorial on how to objectively evaluate patients with motor speech disorders via a common telehealth platform, Zoom. We conducted three tele-evaluations on people with motor speech disorders. From these evaluations, we establish and outline resources for clinicians including evaluation tools and procedures, objective and subjective analysis protocols, and normative values. We discuss three case studies which address diagnoses and potential treatment targets established from the tele-evaluations. Our research shows that tele-evaluations of motor speech disorders can be done efficiently and accurately in real-time to add more certainty to the subjective measures of speech production traditionally used in motor speech evaluations. This research is a viable resource for speech-language pathologists during the COVID-19 pandemic and beyond, as telehealth is likely going to be an increasingly popular service delivery method even after the pandemic. Future studies should compare the results from motor speech evaluations conducted in-person to those conducted via telehealth.

Title: Exploratory Analysis of COVID-19 Case Demographics in Gary, Indiana **Presenter:** Snapp, Cameron

Authors: Cameron Snapp1, Bill Trimoski1, Martin Brown2, Amy Han3, and Tatiana Kostrominova4 1Indiana University School of Medicine; 2 Gary Health Department and Gary Sanitary District; 3Indiana University School of Medicine, Department of Psychiatry; 4Indiana University School of Medicine, Department of Anatomy, Cell Biology and Physiology

Abstract: Health disparities are prevalent in Black and impoverished populations, and COVID-19 is not an exception. Gary, Indiana has a large Black population (80%), high number of residents living below the poverty line (34%), and high unemployment rate (20%). We hypothesized that Black individuals in Gary have a higher rate of positive cases, hospitalizations, and deaths than non-Black individuals. Also, we hypothesized that income (median household income measured by zip code) is negatively correlated with COVID-19 deaths. In collaboration with the Gary Health Department, we analyzed data on all positive cases in the city through 6/19/2020. Data was de-identified and included age, race, ethnicity, and zip code. Data was analyzed using Pearson's chi-square test and regression analysis. Positive cases and hospitalizations are 2-fold and 3-fold more frequent in the Black population compared to the non-Black population in Gary (p<0.0001, P<0.01, age and population-adjusted), respectively. Median household income of a zip code is exponentially and negatively correlated with COVID-19 deaths in that zip code (R2=0.7450, p=0.0123). In Gary, there is a clear health disparity of both income and race, specifically in the context of COVID-19. Officials can utilize this data to reallocate resources to highly populated, low income, and predominantly Black neighborhoods.

COVID-19 & IMMUNOLOGY

Title: Insights from an in vitro derived T Cell Receptor **Presenter:** Alonso, Jesus

Authors: Jesus Alonso1, Nishant K. Singh2, David Kranz3, Brian Evavold4, and Brian M. Baker1 1Department of Chemistry and Biochemistry, Harper Cancer Institute, University of Notre Dame; 2Ragon Institute of Massachusetts General Hospital, Harvard University, and MIT; 3Department of Biochemistry, University of Illinois, Urbana-Champaign; 4Department of Pathology, University of Utah School of Medicine

Abstract: Heterodimeric ab T cell receptors (TCRs) play a key role in cell-mediated immune responses of adaptive immunity. T cells continuously probe peptides presented by major histocompatibility complex (MHC) found on the cell surface. T cell activation initiates through the binding of antigenic peptides on MHCs. Yeast display technology has proven an effective way to gain insight into the underpinnings of peptide-MHC specificity enabling the switching of TCR affinity and specificity to unrelated antigens through directed evolution. Interestingly, in vitro directed evolution also generates mutants that lose peptide specificity. Here, we provide further detail of one of these cross-reactive TCRs, S3-4, which binds tightly but with a highly unusual geometry. Despite binding with an affinity that is characteristic of a strong agonist, S3-4's odd binding geometry does not support T cell signaling. Further investigation with functional experiments and 2D kinetics shows that lack of signaling by S3-4 is ultimately attributable to the TCR's inability to reach ligand. Although S3-4 is an example from a constrained system generated outside the bounds of usual immune function, our results show how unusual binding can influence T cell function and further demonstrate how divergences between 3D and 2D binding parameters can emerge.

12

Title: Determinants of Peptide-MHC Antigenicity for the Development of Personalized/Multiple Peptide Vaccines

Presenter: Keller, Grant

Authors: Grant LJ Keller1, Pramod K Srivastava2, Brian M Baker1; 1Department of Chemistry and Biochemistry and Harper Cancer Research Institute, University of Notre Dame; 2Department of Immunology, University of Connecticut School of Medicine

Abstract: Class I MHC proteins present short peptides to T cells of the immune system. Vaccines incorporating peptides from viruses or containing mutations present in the cancer genome represent a low-cost, broadly applicable type of immunotherapy which can sensitize the immune system to disease, break tolerance, and confer long-lasting immunologic memory with fine specificity. Predicting which candidate neoantigens are likely immunogenic is imprecise, limiting applicability in treating spontaneous disease. We previously demonstrated prediction of immunogenicity from physicochemical characteristics of the peptide in its structural context are more accurate than predictions from sequence-based tools. Our estimation of these characteristics, however, is limited by available three-dimensional structures and the accuracy of computational structural predictions.

In this study, we identified a group of mutant peptides presented in a cancer model and rationalized their immunogenicity with molecular modeling, as predicted peptide binding affinity alone could not explain reactivity. After solving crystal structures of two peptide-MHCs, we developed a method to improve peptide-MHC structural modeling. When evaluated on 93 crystal structures of peptides

bound to the prevalent human class I MHC, HLA-A*02:01, our method demonstrated significantly higher accuracy than conventional model selection. These results are of interest for improving our ability to identify "differences from self" MHC-presented peptides exhibit but are also of translational interest in producing realistic structural and energetic signatures for predicting immunogenicity.

13

Title: The Indiana CTSI PPE Project: A Conduit Between Innovation and Need in the COVID-19 Crisis **Presenter:** Lazarus, Jake

Authors: Jake Lazarus, Indiana University School of Medicine

Abstract: At the onset of the COVID-19 outbreak, the Indiana CTSI partnered with several institutions around the state to ensure PPE needs (and other healthcare industry needs) were being met around the state. This effort was born in response to two main challenges: first, the major PPE manufacturers having to scale their efforts and respond to an overwhelming number of requests from around the country, and second, many smaller organizations and companies who wouldn't normally need PPE not knowing where to find it. Using both public PPE request forms and connecting with organizations who understand local needs (e.g. county health departments, IDOE, etc.), we've worked with our partners, including Ivy Tech Community College, University of Notre Dame and IU Bloomington (to name a few), to distribute 100,000 face masks, almost 50,000 face shields, 15,000 ear guards, as well as printed school desks, Plexiglas sneeze guards, and intubation boxes, among others. As none of the labs who manufactured these supplies traditionally focus on public health, this proves that strong communication between innovative minds and a desire to have a positive impact on the community can lead to swift positive action on a scalable level in times of crises.

14

Title: Delirium Incidence, Duration and Severity in Critically III Patients with COVID-19 **Presenter:** Lindroth, Heidi

Authors: Sikandar Khan2,4, Heidi Lindroth 2,3,4; Jessica Hammes1; Babar Khan2,4,5,6 1Indiana University School of Medicine Indianapolis, IN; 2Division of Pulmonary, Critical Care, Sleep and Occupational Medicine, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN; 3Indiana University School of Nursing, Indianapolis, IN; 4IU Center of Aging Research, Regenstrief Institute, Indianapolis, IN; 5Indiana University Center of Health Innovation and Implementation Science, Indianapolis, IN; 6Sandra Eskenazi Center for Brain Care Innovation, Eskenazi Hospital, Indianapolis, IN

Abstract: COVID-19 is associated with severe respiratory failure and high mortality in critically ill patients.2,4,5 Neurologic manifestations of the disease, including delirium and coma, may also be associated with poor clinical outcomes. Delirium is associated with prolonged mechanical ventilation and mortality.3 This study sought to describe the rates, duration, and severity of delirium in patients admitted to the ICU with COVID-19.

Title: Innate and Adaptive Immune Response to SARS-CoV-2 Infection Play Major Role in Disease Severity

Presenter: Mapader, Tarunendu

Authors: Tarunendu Mapder1*, Sara K. Quinney1,2t, Richard F. Bergstrom1+, Robert E. Stratford1§ 1Division of Clinical Pharmacology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN 46202, USA; 2Department of Obstetrics and Gynecology, Indiana University School of Medicine, Indianapolis, IN 46202, USA

Abstract: The rapid transmission of SARS-CoV-2 in a community is manifested by a wide range of symptoms of coronavirus disease 2019 including fever, pneumonia, acute respiratory distress syndrome and lymphopenia. SARS-CoV-2 infection exhibits fast virus-shedding and long incubation period. Hence, community transmission is faster than disease manifestation and detection of infection. We propose the emergent "cytokine storm" and wrongly posed immune response as the major regulators in disease severity. We calibrated a population of models (POMs) with clinical data for 23 patients across days of symptom onset. The calibration of the POMs is performed by matching the multivariate distributions of the observed data and model outputs. Our model indicates that feedback regulation among the antigen presenting cells, helper T-cells and cytokines contribute to the cytokine pool and T-cell exhaustion. When the adaptive immune response is triggered, B-cells differentiate into plasma cells that produce the IgM and IgG, simultaneously. A decision switch between long- and short-living plasma cells and their conversion was able to model different scenarios of seroconversion. We were able to model viral and immune response following SARS- CoV-2 infection. This model may inform development of intervention strategies through antivirals, monoclonal antibodies, cytotoxic T-cell gene therapy and inhibitors for cytokine receptors.

HEALTH IMPLEMENTATION

Title: Pharmacologic Therapy Among Opioid Exposed Infants: Disparities by Race Presenter: Campbell, Angela

Authors: Angela Campbell, MPH, PhD; Emily Scott, MD, FAAP; Sami Gharbi, MS ECE and Sarah Wiehe, MD, MPH

Abstract: <u>Background:</u> This study examines potential disparities in the receipt of pharmacologic therapy among Black and White infants exposed to opioids in-utero.

<u>Data & Methods</u>: A sample of infants was obtained from a large metropolitan hospital system between 2008-2018 (N=1,760). Exposure was defined as a post-natal NAS/opioid exposure diagnosis or having a mother with an opioid use diagnosis during pregnancy. Logistic regression models were adjusted for insurance status, gender, year of treatment and facility.

<u>Results:</u> Chi-square tests indicate that a smaller proportion of Black infants received opiate weaning relative to white infants and a smaller proportion of Black female opioid users were identified during pregnancy relative White female opioid users. Bivariate and adjusted logistic regressions indicate that Black infants have significantly decreased odds of receiving pharmacologic therapy relative to White infants. This relationship was slightly mediated by the inclusion of a variable indicating whether or not the mother was diagnosed with opiate use during pregnancy.

<u>Conclusion</u>: These results suggest that Black infants have reduced odds of receiving opiate weaning therapy and that this disparity may partly be due to fewer Black female opiate users being identified during pregnancy.

17

Title: Building a Cancer-Related Self-Efficacy Tool for Partners of Breast Cancer Survivors Using Qualitative Interviews

Presenter: Cohee, Andrea

Authors: Andrea Cohee, PhD, Assistant Professor, Indiana University School of Nursing, Claire Draucker, School of Nursing, Indiana University; Victoria Champion, School of Nursing, Indiana University

Abstract: <u>Background:</u> Self-efficacy is a major predictor of physical, psychological, social, and overall quality of life among breast cancer survivors. Because survivor and partner outcomes are often linked, it is reasonable to hypothesize that self-efficacy is an important predictor of physical, psychological, social, and overall QoL in partners as well. However, this hypothesis has yet to be tested, in part because no scale exists to measure partners' cancer-related self-efficacy. Development and psychometric testing of such a scale is a critical first step in developing a theoretical model predicting QoL in this population.

<u>Methods</u>: Our first step following standard instrument development procedures is to interview partners using open-ended questions. Partners are asked about the challenges they faced during treatment, following treatment, and how they have coped with those challenges.

<u>Results</u>: Data collection is ongoing with 11 of 20 interviews completed. Partners (N=11) identified over 35 issues that hampered their confidence in dealing with breast cancer. The main domains of 1) providing support to spouse, 2) navigating the medical system and treatment options, 3) coordinating family and friends, 4) managing the household, and 5) dealing with their own emotions.

Discussion: Once data collection is finished; a scale will be finalized with all identified challenges.

Title: Feasibility of Parent Navigators for Parents of Justice-Involved Youth **Presenter:** Dir, Allyson

Authors: Allyson Dir, PhD, Department of Psychiatry, Indiana University School of Medicine; Sarah E. Wiehe, MD, MPH, Department of Pediatrics, Indiana University School of Medicine; Matthew C. Aalsma, PhD, Department of Pediatrics, Indiana University School of Medicine

Abstract: Parental engagement in youth services is crucial for positive youth development; however, across service systems parental engagement is challenging. Peer specialists, or those with lived experience, are effective in increasing treatment engagement among other populations and may increase parental engagement in youth services. The current project seeks to develop, implement, and examine the preliminary feasibility and acceptability of a parent peer navigator intervention to improve service use and outcomes among justice-involved youth. Utilizing community-based participatory research, I will collaborate with the Marion County Juvenile Court and community advisory board to develop a parent peer navigator intervention protocol. Following training of n=2 parent peer navigators, I will conduct a feasibility study to program intervention feasibility and acceptability. Guided by the Exploration, Preparation, Implementation, and Sustainment (EPIS) framework, qualitative and quantitative data will be collected from juvenile justice staff, advisory board, and parents to measure feasibility and implementation outcomes.

19

Title: Health Disparities in Lung Cancer Diagnosis and Treatment: A Single Center Retrospective Study from a Central Indiana Hospital

Presenter: Duncan, Fancesca

Authors: Francesca Duncan, MD MS1; Andrew Killion1; Nawar Al Nasrallah, MD1; Ahmad Al-Hader, MD2; Catherine Sears, MD1; Indiana University School of Medicine Division of Pulmonary & Critical Care Medicine1; Indiana University School of Medicine Division of Hematology and Oncology2

Abstract: Lung cancer is the leading cause of cancer-related mortality in the United States for men and women. African Americans are disproportionately affected with lung cancer, having higher incidence and mortality rates compared to Caucasian men and women. Several studies are looking for genetic differences to explain the etiology of the disparity, while others are examining how socioeconomic and environmental factors contribute to lung cancer disparities. Current lung cancer screening guidelines have recently shown that high risk African Americans may be missed based on current guidelines. This retrospective study was designed to analyze demographic features, including stage at diagnosis, treatment, and mortality, to assess potential reasons for the disparity that exist. 3400 lung cancer patients from January 2000 – May 2015 were reviewed from the IU Simon Cancer Center Registry. We hypothesized that African Americans would have increased mortality, higher lung cancer stage at the time of diagnosis, and less timely, stage appropriate treatment. Our study showed that African Americans had less time between time of diagnosis and death compared to Caucasians. We also showed that African Americans had less stage appropriate treatment compared to Caucasians for all lung cancer stages. Further studies will seek to examine potential reasons for these differences.

Title: Tracking the Process of Treatment Seeking in Breast Cancer Patients **Presenter:** Hayes, Lisa

Authors: Jennifer Leising1,3, Shangyuan Ma1,3, Lisa Hayes2, Cleveland Shields1,4, Poching DeLaurentis1, Yuehwern Yih1,3; 1Regenstrief Center for Healthcare Engineering, Purdue University; 2R.E.D. Alliance, Indianapolis, IN; 3School of Industrial Engineering, Purdue University; 4Department of Human Development & Family Studies, Purdue University

Abstract: Higher mortality in Black versus White breast cancer patients is a historical and continuing problem across the United States, including in Indiana. The cancer incidence rate has converged but the mortality rate has increased in the past decades. Black women are also diagnosed at a later disease stage than White women. This study examines variability in the process of care seeking and care receipt for Black versus White patients. We seek to understand the process through which Black versus White patients obtain screenings and diagnoses and move along the continuum of care through treatment. We will interview Black and White breast cancer survivors to map a care timeline and to identify barriers to care, if any, that impeded their progression through the breast health continuum of care. Our goal is to identify critical paths in the care system and set target performance in those areas to achieve systemic improvement in accessibility and delivery of breast health services. The ultimate goal of this project is to eliminate unnecessary delay and missed opportunities for care, thereby reducing the mortality rate disparity.

HEALTH IMPLEMENTATION II

Title: Developing a Multilevel Intervention to Increase Hepatitis C Virus Screening of Baby Boomers in Primary Care **Presenter:** Kasting, Monica

Authors: Monica L. Kasting, PhD, Cleveland G. Shields, PhD, Susan M. Rawl, PhD

Abstract: The worldwide incidence of liver cancer increased 75% from 1990 to 2015 due, in part, to chronic hepatitis C virus (HCV) infection. Individuals born 1945-1965 (baby boomers) have five times the prevalence of HCV infection compared to other birth cohorts, but fewer than 15% of this cohort have been screened. Effective interventions to increase HCV screening among baby boomers are urgently needed. In partnership with a provider advisory board and a community advisory board, we will develop a multilevel intervention targeting both providers and patients in primary care. We will assess the feasibility, acceptability, and usability of the intervention among patients and providers. While the specific content of both intervention components will be finalized at the completion of the study, we envision that the provider-level intervention will likely include a one-time education session and monthly performance feedback e-mails regarding their HCV screening rates. The patient-level intervention may include reminder post-cards and clinic-based education, engagement, and activation. The long-term goals of this project are to: 1) develop an acceptable, feasible, and usable multilevel intervention aimed at increasing HCV screening in primary care; and 2) understand the relationship between the intervention components and HCV screening; and 3) reduce HCV-related morbidity and mortality.

22

Title: Priority-setting for Cochrane Review Updates with Clinicians and Consumers **Presenter:** Kumar, Nimisha **Authors:** Nimisha Kumar, BS; David M Haas, MD, MS, Sean Grant, DPhil, MSc

Abstract: Introduction: The US Satellite of the Cochrane Pregnancy & Childbirth Group was launched in March 2019. One of the goals of the US-PCG was to engage both clinicians and consumers in a priority-setting exercise that aimed to (1) identify which systematic reviews to update and (2) reveal any gaps in current knowledge that require a new review. Methods: A series of editorial team evaluations narrowed a list of over 600 relevant review titles down to 97, all of which were in 7 topic categories. A Qualtrics survey was used. Respondents selfidentified as a clinician/researcher or consumer and then were asked to rank 10 titles as "highest priority" and another 20 as "medium priority." This survey was disseminated through various channels, including ACOG, March of Dimes, Cochrane, and social media networks. Results: 63 participated in our survey, with 45 clinicians and 18 consumers. Of the 7 categories, maternal medical problems, and complications (MMPC) was the topic of most interest overall (79.4%). MMPC was chosen most by clinicians but was tied with psychosocial factors in postpartum care (PFPC) for consumers. Antiplatelet agents for preventing preeclampsia was the only title in the top 3 priority by both clinicians and consumers, but multiple titles overlapped in the top 10 priority. Conclusions/Implications: Clinicians and consumers were able to select priority titles for updating reviews with the groups often sharing some consensus. Stakeholder consensus on review topics will be further refined using Delphi methods to a final priority list by the end of 2019.

Title: Low-risk Adenoma Surveillance Decision-making: Perspectives from Patients and Providers **Presenter:** Maratt, Jennifer

Authors: Jennifer K. Maratt, MD, MS1; Mentors: Thomas Imperiale, MD1, Marianne Matthias, PhD1, 1Department of Medicine, Indiana University School of Medicine; Richard L. Roudebush VA Medical Center; Regenstrief Institute, Inc.

Abstract: <u>Background:</u> A large proportion of colonoscopies are performed for post-polypectomy surveillance. Data show that there is underuse of surveillance for high risk colon adenomas, but overuse for low-risk adenomas (LRAs). Overuse can be attributed to patient, provider, and system-level factors yet little is known about patients' beliefs and understanding of colorectal cancer risk in the setting of LRAs. Endoscopists recommend future colonoscopies primarily based on polyp characteristics, not taking into account patient health status or preference. On the other hand, primary care providers (PCPs), who are aware of these factors, rarely deviate from endoscopists' recommendations. The primary objective of this study is to obtain an in-depth understanding of the decision-making process for LRA surveillance from patient and provider perspectives. <u>Methods:</u> Using semi-structured interviews, a total of 32 patients with a history of LRAs and 16 providers (PCPs and gastroenterologists) from Roudebush VA and Eskenazi will be interviewed. The following domains will be covered: risk communication, risk perception, and decision-making for LRA surveillance. A 3-phase approach, immersion, reduction, and interpretation, will be used to collect and analyze data.

<u>Potential Impact</u>: Understanding decision-making for LRA surveillance colonoscopy has the potential to inform future interventions targeted towards reducing overuse of this low-value service.

24

Title: Doctors and Patients and Parents, Oh My!: A Translational Case Study with Diverse Stakeholders for a Patient Decision Aid from Development to Implementation **Presenter:** Panoch, Janet **Authors:** Janet Panoch, PhD, Indiana University School of Medicine

Abstract: Patients diagnosed with osteosarcoma in the lower extremity often have the option to choose between amputation, limb salvage surgery with endoprosthesis, or rotationplasty, in which the ankle and foot are rotated and transplanted to the femur. Each has a very different appearance and functional ability. Long-term outcomes, potential complications, and mobility limitations are uncertain and largely omitted in patient-provider consultations.

An interdisciplinary team has been assembled to develop content using advanced technology for an online, interactive patient decision aid. The International Patient Decision Aid Standards (IPDAS) include needs assessments with both patients and providers prior to development. IPDAS requirements also include discussion of the potential risks and benefits for each option and realistic personal stories with long-term patient-reported outcomes.

Breakout groups in the form of task forces for orthopedic surgeons, oncologists, rehabilitation professionals, decision-making experts, and osteosarcoma community members will discuss key decision points and pathways for information dissemination to youth, adults, and parents for decision-making. The product will be pilot tested and beta tested and has implications for orthopedic education changes from the "saving-the-leg" gold standard to shared decision-making.

This project is funded by a five-year NIH grant between the Amputee Coalition and the Administration for Community Living.

25

Title: Enrollment of Diverse Populations in the INGENIOUS Clinical Trial Presenter: Williams, Ebony Authors: E Shah-Williams, KD Levy, Y Zang, AM Holmes, C Stoughton, P Dexter, TC Skaar

Abstract: Recruitment of diverse populations and subjects living in Medically Underserved Areas and Populations (MUA/P's) into clinical trials is a considerable challenge. To identify enrollment variables that predict enrollment in a diverse underserved population, we analyzed data from the INGENIOUS, (Indiana GENomics Implementation and Opportunity for the UnderServed), pharmacogenomics clinical trial conducted at a community hospital for underserved subjects (Safety net hospital,) and a statewide healthcare system (Academic hospital). We used a logistic regression model to identify patient variables that predicted successful enrollment after subjects were contacted and evaluated the reasons that clinical trial eligible subjects refused enrollment. In both healthcare systems, African Americans were less likely to refuse the study than non-Hispanic Whites (Safety net, OR =0.68, p<0.002; Academic hospital, OR=0.64, p<0.001). At the Safety net hospital, other minorities were more likely to refuse the study than non-Hispanic Whites (OR=1.58, p<0.04). The odds of refusing the study once contacted increased with patient age (Safety net hospital, OR=1.02, p<0.001, Academic hospital, OR=1.02 p< 0.001). At the Academic hospital, females were less likely to refuse the study than males (OR=0.81, p=0.01) and those not living in MUA/P's were less likely to refuse the study than those living in MUA/P's (OR=0.81, p=0.007). The most frequent barriers to enrollment included not being interested, being too busy, transportation, and illness. In conclusion, African Americans can be readily recruited to pharmacogenetic clinical trials once contact has been successfully initiated. Enrollment could be further enhanced by improving research awareness of clinical trials, including diverse recruiters who represent the communities they enroll, reducing time needed for participation, and compensating for travel.

MICROBIOLOGY & IMMUNOLOGY

Title: Investigation of a Series of 1,4-diaryl-pyrazolo-pyridinones as Anti-Leishmanial Agents **Presenter:** Corman, Hannah

Authors: Hannah N. Corman1, Douglas A. Shoue1, Bruce J. Melancon2, and Mary Ann McDowell1; 1Eck Institute for Global Health, University of Notre Dame; 2Vanderbilt Center for Neuroscience and Drug Discovery, Vanderbilt University

Abstract: Leishmaniasis is a grouping of diseases caused by the protozoan parasites Leishmania spp., affecting 12 million people per year with almost 310 million people at risk. Leishmaniasis has a range of clinical manifestations, from self-healing skin lesions to fatality. Chemotherapies like intravenous pentavalent antimonials are highly toxic, while oral treatment options such as paromomycin and miltefosine have been used more as incidences of disease relapse and drug resistance develop, emphasizing the importance of identifying new and effective chemotherapies. We developed a novel, target—free fluorometric high-throughput screen (HTS) to identify small molecules with anti-leishmanial activity. Screening of 10,000 small molecules from the ChemBridge DIVERset-EXPTM library yielded 210 compounds that killed 80 percent of parasites, resulting in a hit rate of 2.1 percent. One hundred nine (109) molecular scaffolds were represented within the hit compounds; one scaffold that exhibits potent anti-leishmanial activity was 1,4-diaryl-pyrazolopyridinone (1,4-DAPP). A total of 27 novel 1,4-DAPP compounds were synthesized and antileishmanial efficacy and host cell toxicity was determined using L. donovani mCherry expressing amastigotes and THP-1 macrophages; successful drug treatment was considered when the IC50 value was less than 10µM and the CC50 value was greater than 50µM. Future studies include in vitro and in vivo characterization of these novel compounds.

27

Title: Evaluating the Effect of Prebiotics on the Gut Microbiome Profile and β -cell Function in Newly-Diagnosed Type 1 Diabetes

Presenter: Ismail, Heba

Authors: Heba Ismail, MD, Indiana University Purdue University Indianapolis; Carmella Evans-Molina, MD, PhD; Linda A DiMeglio, MD, MPH Department of Pediatrics, Indiana University School of Medicine

Abstract: Type 1 diabetes (T1D) results from the autoimmune destruction of insulin-producing β cells. Emerging data suggest that differences in intestinal microbiota might be critically involved both in autoimmunity and in glucose homeostasis. The prebiotic high amylose maize starch (HAMS) alters the gut microbiome profile and metabolites positively by increasing production of beneficial short chain fatty acids (SCFAs) that have significant anti-inflammatory effects. It also improves glycemia, insulin sensitivity and secretion in healthy non-diabetic adults. Further, an acetylated and butyrylated form of HAMS (HAMS-AB) that increases beneficial SCFA production, namely acetate and butyrate, has been safe and effective in disease prevention in mouse T1D models. The objective of the proposed study is to assess the effect of administering a prebiotic, such as HAMS-AB, on the gut microbiome profile, SCFA production, glycemia and β -cell function in humans with T1D. Here we hypothesize that administration of HAMS-AB will (i) improve the gut microbiome profile in humans with T1D, (ii) increase SCFA production, and (iii) improve β -cell function, β -cell health and overall glycemia. We propose a pilot randomized controlled cross-over trial of HAMS-AB in 12 youth with newly-diagnosed T1D. We will use state-of-the-art markers to profile the gut microbiome (using 16S rRNA sequencing), measure stool SCFA levels (using gas chromatography), asses β -cell stress/death (by measuring proinsulin to C-peptide ratios) and glycemia (assessed by continuous glucose monitoring and HbA1c measurements). We have thus far enrolled two participants in this study. We expect that the use of HAMS-AB in newly diagnosed youth with type 1 diabetes will alter the gut microbiome profile (thus increasing the number of fermenters and SCFA levels), glycemia and β -cell function in humans with T1D.

28

Title: Computational Model of Ebolavirus Matrix Protein Assembly Phospholipid Influence on Production of Viral Particles

Presenter: Liu, Xiao

Authors: Liu X1,*, Pappas E1,*, Husby ML2, Stahelin RV2, Pienaar E1; 1Weldon School of Biomedical Engineering; 2Department of Medicinal Chemistry and Molecular Pharmacology, Purdue University

Abstract: Ebola virus (EBOV) causes severe hemorrhagic fever in humans, with up to 90% mortality rates without treatment[1]. EBOV studies are limited by the BSL4 requirement for work with live viruses. However, EBOV matrix protein VP40 alone can assemble into virus-like particles (VLPs)[2], making it a useful model system for studying EBOV budding processes in BSL2 facilities. To study VLP dynamics, and evaluate phosphatidylserine-targeted treatment, we built an ODE-based mathematical model of the VP40 system. Phosphatidylserine plays an important role in VLP budding[3,4], and our model predicts that it most strongly affects binding of VP40 dimer to cell membrane, budding of mature filaments as well as stabilization of filaments. Stabilization of filaments has not been shown for EBOV, but similar mechanisms have been identified in oligomerization of microtubules[5]. Our results also suggest that the effect of PS on budding depends on the state of the system and the parameter space, which explains why the decrease of PS in some, but not all, experiments leads to decrease of VLP. The model is poised to consider additional viral proteins, more cell component interactions, dose-response predictions for drugs that affect membrane PS concentration, and mechanism identification for drug discovery in parallel with experimental studies.

29

Title: Antimicrobial photodynamic therapy of Staphylococcus aureus using non-iron hemin analogs **Presenter:** Sivasubramaniam, Badhu

Authors: Benjamin Washer *, Badhu Sivasubramaniam*, Yuichiro Watanabe*, Alex Wei*

* Department of Chemistry, Purdue University, West Lafayette, Indiana 47907

Abstract: Antimicrobial photodynamic therapy (aPDT) utilizes photosensitizers (PS) to generate bursts of singlet oxygen and other reactive oxygen species (ROS) upon visible-light irradiation1. Non-iron metallo- protoporphyrins mimicking hemin have effective antimicrobial activity against both Gram-positive and - negative bacteria.2 Our lab has established that PS based on protoporphyrin IX (PpIX) derivatives with non- iron centers (AI-PpIX, Ga-PpIX, In-PpIX) are more potent than other PS such as TmPyP.3 Our recent studies with silver nanoparticle conjugated Ga-PpIX unit, stabilized by hemoglobin have shown higher aPDI activity compared to Ga-PpIX itself.4 These PS are taken up within seconds by S. aureus and MRSA, attributable to direct uptake mechanisms via cell-surface hemin receptors, namely iron-regulated surface determinant (Isd) proteins. The PpIX derivatives appear to have differences in their mechanism of action against S. aureus, dominated either by generation of singlet oxygen or other ROS. Al-PpIX and Ga-PpIX have more potent aPDT activity

against S. aureus than In-PpIX, with 3-log reduction in CFU/mL at 0.03 μM after a 30-second irradiation using a 405-nm LED source. aPDT mediated by photoactive hemin analogs can be a potential alternate therapy for many multidrug-resistant pathogens that actively express hemin acquisition systems, and a are promising method for treating topical and oral bacterial infections.

30

Title: Mycobacterium avium Infection in the Lungs: An Agent-based model showing the Effects of Bacterial Phenotypes and Biofilm

Presenter: Weathered, Catherine

Authors: 1Catherine Weathered*, 2Patricio Escalante, 2Kelly Pennington, 1Elsje Pienaar 1Purdue University, West Lafayette, IN, USA, 2Mayo Clinic, Rochester, MN, USA

Abstract: Mycobacterium avium complex (MAC), a type of nontuberculous mycobacteria, are environmental microbes, capable of colonizing and infecting humans following inhalation of the bacteria. We hypothesize a balance of bacterial factors (phenotypic diversity and biofilm formation) and host immune factors (speed and magnitude of response) is key to establishing and prolonging these notoriously difficult to treat infections in the lung. To test these hypotheses, we developed a 3D agent- based model (ABM) that incorporates known interactions between bacteria, biofilm and immune cells in virtual lung tissue.

Model results show an early relationship between the initial number of macrophages or distance that chemoattractants diffuse, and the ratio of planktonic to sessile bacteria. Though larger initial macrophage numbers result in a stronger reduction in planktonic bacteria early after infection, sessile bacteria within biofilms and infected macrophages can sustain the bacterial population, allowing the planktonic population to recover. This effect is offset with further chemoattract diffusion, as the macrophages can clear the infection early or recruit more macrophages. Thus, the model predicts that both bacterial phenotypes and a suppressed immune response affect the bacterial ability to survive, propagate, and establish infections. Future directions include adding drug pharmacodynamics and the role of phenotypes in cell-level pharmacodynamics.

MODELING

Title: Medication Use Safety During Care Transitions for Children with Medical Complexity **Presenter:** Abebe, Ephrem

Authors: Ephrem Abebe, PhD, Purdue University, Department of Pharmacy Practice, West Lafayette, Indiana

Abstract: Children with medical complexity (CMC) are a medically fragile and growing member of the pediatric patient population. Their medical care spans multiple healthcare professionals and care settings. Consequently, CMC experience frequent transitions of care and are at increased risk for medication related harm. Such risks are poorly understood and represent a major patient safety gap. Aims: of this study are: (1) to understand care transition-related medication safety risks for CMC, and (2) through a participatory design (PD) approach, to develop an early prototype intervention to address identified safety risks. Methods: For Aim 1, guided by System Engineering Initiative for Patient Safety 2.0 framework, we will conduct observations (with clinicians) and semi-structured interviews (with 5 family caregiver dyads each) during three care transition experiences: from Cardiac ICU to home, Neonatal ICU to home, and those between primary care/specialty clinic to home. Observation notes and transcribed interviews will be analyzed using accepted qualitative data analyses methods. For Aim 2, we will conduct PD sessions with up to 5 participants (separately for clinicians and family caregivers) from each of the three care transition types. Expected Outcome: Early prototype tool will inform future planned study aimed at evaluating its effectiveness.

32

Title: Population pharmacokinetics of R and S methadone in children undergoing major surgery **Presenter:** Aruldhas, Blessed

Authors: Blessed W. Aruldhas1,3, Brian R. Overholser1,2, Sara K. Quinney1, Andrea R. Masters1, Christine M. Bach1, Senthil Sadhasivam1; 1Indiana University School of Medicine, Indianapolis, IN; 2Purdue University College of Pharmacy, Indianapolis, IN; 3Christian Medical College, Vellore, India

Abstract: <u>Objectives:</u> Methadone is a racemic synthetic opioid used for postoperative analgesia in addition to its widespread use in opioid abuse disorder. The individual enantiomers vary in their pharmacokinetic and pharmacodynamic properties. The optimal dose required to achieve therapeutic concentrations for effective analgesia in children is not fully known.

<u>Methods:</u> Methadone was given to 38 children both intravenously in the operating room and orally at a dose of 0.05 to 0.1 mg/kg every 12 hours. Blood samples were collected on multiple occasions over 3 to 5 inter-dose intervals. R-methadone, S-methadone and AAG (acid alpha glycoprotein) concentrations were measured using liquid chromatography. The pharmacokinetic data were analyzed using a nonlinear mixed effect modeling approach in NONMEM(v7.4) using FOCE method with interactions.

<u>Results:</u> The pharmacokinetics of both R and S-methadone were described by two-compartment disposition models with linear elimination and first order absorption. AAG (alpha-acid-glycoprotein) was identified as a covariate on central volume for both the enantiomers (Δ OFV = 11.5 and 12.4 respectively). Visual predictive checks and bootstrapping validated the present model. <u>Conclusions:</u> Pharmacokinetic models were successfully created for both R and S methadone in children. AAG and BMI were important covariates describing the volume of central compartment in

Title: Closing the Cross-institutional Referral Loop:Assessing consultant notes **Presenter:** Savoy, April

Authors: April Savoy, PhD1,3,4, Amee Sangani2, and Michael Weiner, MD, MPH2,3,4; 1Purdue School of Engineering and Technology, 2Indiana University School of Medicine, 3Center for Health Information and Communication, U.S. Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development Service CIN 13-416, Richard L. Roudebush VA Medical Center, 4Regenstrief Institute, Inc.

Abstract: <u>Objective:</u> Poor communication and co-management of comorbidities during the referral process increases physician workload, patient burden, and risks. In this preliminary study, our objective was to understand how consultants' notes support physician collaboration within and across health care institutions.

<u>Project Methods:</u> We conducted chart reviews. Accessing the Indiana Network for Patient Care database, consultation notes were randomly selected from five specialties within the Indiana University Health network, including internal and external referrals. The Quality of Consult Assessment tool was adapted to assess note quality and co-management facilitation. <u>Results:</u> We reviewed medical records of ten patients. All consultation notes contained clinical recommendations. Seventy percent of notes referred to explicit consultant responsibilities. Conversely, only one contained explicit responsibilities for referrers. Charts denoted reliance on support staff to send messages among referrers, consultants, and patients via phone and facsimile. <u>Conclusion:</u> The clinical documentation reviewed supported specialty referrals for transitions of care rather than co-management of care. Accessing medical records across institutions contributed to a lack of clinical context, and workflow inefficiencies, when attempting to co-manage clinical care.

34

Title: Computational Modeling of Dermal Replacement Therapy for Difficult-to-Heal Wounds **Presenter:** Sohutskay, David

Authors: David O. Sohutskay1,2, Adrian Buganza Tepole1,3, Sherry L. Voytik-Harbin1,4; 1Weldon School of Biomedical Engineering, Purdue University, West Lafayette, IN 47907; 2Indiana University School of Medicine, Indianapolis, IN 46202; 3Department of Mechanical Engineering, Purdue University, West Lafayette, IN 47907; 4Department of Basic Medical Sciences, Purdue University, West Lafayette, IN 47907

Abstract: <u>Aim:</u> Difficult-to-heal wounds lead to displeasing cosmetic outcomes and also carry a high burden of scarring, contracture, or amputation due to nonhealing. There exists a need for regenerative dermal replacement strategies that adapt and grow with the individual, but a continuing challenge is identification of optimal scaffold parameters for healing. We present a new computational model for prioritization of collagen scaffold design parameters for dermal regeneration.

<u>Methods</u>: In previous animal experiments, we evaluated dermal replacement scaffolds customfabricated from fibril-forming collagen oligomer with controlled fibril density in rat excisional wounds. We now parameterize the scaffold parameters in representative constitutive laws and developed a chemo-bio-mechanical finite element model including collagen, cells, and cytokine signaling to simulate wound healing. <u>Results:</u> Collagen microstructure was quantified from scanning electron micrographs. A constitutive law for collagen mechanics was fit to uniaxial tensile tests. Using this information, we conducted preliminary three-dimensional finite element model simulations of wound contraction, recellularization, and collagen remodeling. We will iteratively inform the model by comparing computational model predictions with actual experimental outcomes.

<u>Conclusions</u>: We developed a mechanobiological computational model of wound healing. The model will be used to explore cell-scaffold interactions for purposes of prediction and optimization of tissue regeneration outcomes.

35

Title: Utilization of Speech Analysis as a Diagnostic Tool to Objectively Evaluate Early Signs of Medical Conditions and Recovery
Presenter: Stokes, Michael
Authors: Michael A. Stokes, Waveform Communication, LLC

Abstract: The Waveform Model of Vowel Perception and Production explains the intricate coordination of the lips and tongue for the production of American English vowels. When a person misses the typical articulatory targets or timing of vowel productions, this can be reflective of a neurological or physical impairment. In collaboration with Methodist Sports Medicine, patients were recorded to identify patterns indicative of neurological impairment from concussion. With Regenstrief Institute, speech recordings were added to an observational study conducted to monitor and detect the onset of altered level of consciousness and delirium in patients after a major non-cardiac thoracic surgery. Each of the 45 concussion subjects, 16 delirium study subjects, and 20 control subjects were recorded on at least 2 separate days allowing for the talker's speech to be compared to their own productions to investigate differences that may reflect impairment and recovery. Over 4,000 vowels produced in coarticulatory neutral h-vowel-d words (had, hid, etc.), and over 150,000 rows of data of impaired speech have been collected across the studies. The results have been enlightening and indicative of impairment providing motivation for both studies to go beyond the pilot, and other medical conditions are being considered for study including COVID-19.

NEUROSCIENCE I

Title: HYPE-mediated AMPylation as a novel therapeutic target for neurodegeneration Presenter: Camara, Ali

Authors: Ali Camara, Laboratory of Dr. Seema Mattoo, Dept. of Biological Sciences-Purdue University, West Lafayette, Indiana

Abstract: A major hallmark of Parkinson's disease (PD) is the deposition of the intrinsically disordered protein α -synuclein (α Syn) into intracellular inclusions termed Lewy bodies. We previously reported that HYPE/FicD—the sole human homolog of the Fic family of adenylyltransferase enzymes — covalently adenylylates (AMPylates) α Syn in vitro. HYPE-mediated AMPylation ameliorates many of the neurotoxic phenotypes of α Syn implicated in the progression of PD, such as α Syn fibrillation and membrane permeability. These potentially cytoprotective phenomena conferred by HYPE's adenylyltransferase activity make it an attractive therapeutic target. We therefore set out to screen both FDA-approved and proprietary small-molecule compound libraries towards the identification of novel manipulators of HYPE AMPylation. Employing the fluorescence polarization of an ATP analog fluorophore—FI-ATP—we developed and optimized an efficient, robust assay which monitors HYPE autoAMPylation and is amenable to automated, high-throughput processing of diverse chemical libraries. Challenging our pilot screen with compounds from the LOPAC, Spectrum, MEGx, and NATx libraries yielded 0.3% and 1% hit rates for HYPE activators and inhibitors, respectively. Further, these hits were assessed for dose-dependency and validated via orthogonal biochemical AMPylation assays. We thus present a high-quality HTS assay suitable for tracking HYPE's enzymatic activity, and the first small molecule manipulators of HYPE-mediated AMPylation.

37

Title: Gender Differences in Impulsivity on Youth at Risk for Substance Use Disorders Presenter: Chimelisii-Santiago, Jose

Authors: José R. Chimelis-Santiago, MS, Ya Chai, Leslie Hulvershorn, MD

Abstract: This study objective was to assess the gender differences in impulsivity and psychiatric disorders in youth at risk for substance use disorders. This study analyzed the data obtained from a longitudinal neuroimaging research project. The sample (males n = 56 / females n = 56) were youth with disruptive behavior disorders (attention/deficit-hyperactivity disorder, oppositional defiant disorder, conduct disorder and unspecified disruptive behavior) matched on age, IQ, race, parental education, parental substance use, psychotropic medication use and trauma history. Impulsivity was measured by the UPPS-P-C, which assesses impulsivity distinguished by five components: urgency, lack of premeditation, lack of perseverance, positive and negative urgency, and sensation-seeking. Mood disorders were assessed by the KSADS-PL. Significant gender differences were found in the total score of the UPPS-P-C (p = .003). Overall, male subjects demonstrated more impulsivity compared to females. Particularly, sensation seeking (p = .002) and lack of premeditation (p = .019) subscales drove those differences. Females had more lifetime affective disorders compared to males, specifically a greater proportion had past major depressive disorder (p = .042) and current anxiety disorders (p = .042). The next steps of the project will be to examine gender differences on neural responses to risky decision making.

Title: MOBILE clinical trial - Autologous Bone Marrow Cell Therapy Reduces Opioid Dependence in Patients with Critical Limb Threatening Ischemia

Presenter: Couetil, Justin

Authors: Justin L. Couetil1, Michael P. Murphy2; 1Indiana University School of Medicine; 2Indiana University School of Medicine, Department of Vascular Surgery

Abstract: Critical limb-threatening ischemia (CTLI) can be considered the "heart attack of the leg". Pain is so severe that patients require amputation and have a high-risk for opioid addiction; moreover, up to a third of patients do not have the option of traditional revascularization procedures. The MOBILE trial investigated autologous stem cells (ABMNC) to improve 1-year amputation-free survival in these no-option patients. Though overall ABMNC effect was not significant, (P = 0.143), non-Diabetic patients benefitted from cell therapy (P = 0.009, HR = 0.3, CI = 0.12-0.79), as well as Rutherford 4 patients (P = 0.036, HR = 0.29, CI = 0.22-0.36). Diabetic and Rutherford 5 patients saw no reduction in amputation. Among those receiving ABMNC therapy who survived the year amputation-free, quality of life pain ratings improved for non-Diabetic patients (P < 0.001), stagnated for Diabetic patients (P = 0.21), and both Rutherford 4 and 5 patients improved (P < 0.01). Controls did not improve, and no groups were significantly different at baseline. Patients receiving cell therapy had fewer opioid prescriptions (P < 0.01). Cell therapy can meet the urgent need to prevent amputations and reduce opioid requirements for certain no-option CTLI patient populations.

39

Title: The Role of Alcohol in Hippocampal Calcium Channel (Cav1.2) expression **Presenter:** Kokoska, Ryan

Authors: Ryan Kokoska1, Eric Rodriguez2, Bryan Yamamoto2; 1Indiana University School of Medicine; 2Indiana University School of Medicine, Department of Pharmacology and Toxicology

Abstract: <u>Background and Hypothesis:</u> L-type calcium channels (including Cav1.2) play important roles in hippocampal glutamatergic neurotransmission underlying memory and learning. Their overexpression is implicated in cell death and chronic alcoholism. While increases in hippocampal Cav1.2 gene expression have been reported following chronic involuntary ethanol exposure, the regional distribution has not. We hypothesize that the expression of hippocampal Cav1.2 channels is increased by EtOH drinking in a region-specific manner.

<u>Methods</u>: Male Sprague Dawley rats were allowed 28 days of intermittent access to 10% EtOH solution. 24 hours after last exposure, brains were collected and processed for

immunohistochemistry. Cav1.2-associated immunofluorescent signal from hippocampal subregions was quantified using ImageJ analysis software.

<u>Results:</u> Immunohistochemical results indicate that Cav1.2 immunoreactivity in the hippocampal stratum granulosum layer within the Dentate Gyrus and the stratum pyramidale layer within CA1 and CA3 regions was increased in response to EtOH treatment. There was no significant change for the CA2 region.

<u>Conclusion</u>: This study suggests that calcium signaling in hippocampal subregions is differentially affected by EtOH consumption, which may contribute to calcium-mediated apoptosis.

<u>Impact and Implications</u>: Understanding the process of EtOH-induced hippocampal calcium signaling presents opportunities for understanding the consequences of chronic alcohol exposure related to hippocampal function, and possible interventional therapies.

40

Title: TBI-on-a-chip: Linking physical impact to neurodegeneration by deciphering primary and secondary injury mechanisms

Presenter: Rogers, Edmond

Authors: Edmond A. Rogers1,2,3, Timothy Beauclair1,2, Guenter W. Gross3, and Riyi Shi1,2; 1Department of Basic Medical Sciences, School of Veterinary Medicine, Purdue University, West Lafayette, IN 47907; 2Weldon School of Biomedical Engineering Purdue University, West Lafayette, IN 47907; 3Department of Biological Sciences and Center for Network Neuroscience University of North Texas, Denton TX 76203

Abstract: We have engineered a highly-novel, primary culture-model to reproduce clinicallyrelevant g-forces with unprecedented temporal and spatial resolution for mechanistic investigations into post-TBI (traumatic brain injury) neurodegeneration.

Using neuronal networks grown on multielectrode-arrays with a pendulum-injury device and standard immunofluorescent methods, we noted significant, force-dependent increases in the ROS acrolein at 24hrs post-impact, indicative of post-impact neuronal degeneration. These changes were amplified by the following: exposure to higher g-forces (30-250g, peak); the rapid (4-6sec interval) application of multiple impacts (1,3,5 and 10x); and exposure to 40mM EtOH for a 10min duration immediately following impact. Further, we demonstrate the enhancement of injury-recovery as a function of increasing time intervals between repeated hits. In addition, conditioned media from maximally-impacted cultures can cause acrolein elevation when introduced to non-impact, control networks, indicating acrolein's role as a diffusive-factor in post-TBI secondary injuries. This model recreates trauma with sub-cellular resolution and has the ability to separate primary and secondary injuries. With this newly established in vitro tool, combined with our available in vivo models, we expect to gain insight into the mechanisms underpinning TBI (acute and chronic) and its link to neurodegeneration, helping to guide our translational laboratory endeavors and improving clinical diagnoses and treatments.
NEUROSCIENCE II

41

Title: Collaborative Care for Opioid Dependence and Pain (CCODAP) Presenter: Bushey, Michael Authors: Michael A. Bushey, MD, PhD, Assistant Professor of Psychiatry, Indiana University School of Medicine

Abstract: The use of opioid pain medications to treat chronic pain has led to widespread opioid dependence and an exponential rise in drug overdose deaths. Tapering of opioids is desirable but challenging in primary care and specialty clinics that lack behavioral health expertise. To provide critical support to patients and providers during opioid medication tapering, we propose to enroll 40 patients into a randomized pilot clinical trial of a 12-week telecare collaborative care program administered by a psychiatrist and peer recovery specialist team. The intervention will incorporate a positive psychology intervention for treating chronic pain. Our primary aim is to determine the potential effectiveness of our intervention in facilitating opioid medication weaning, with reduction in opioid dose as the primary outcome. Our secondary aims are to assess pain outcomes, patient satisfaction, and barriers to adherence. The results from this feasibility study will inform a larger randomized control trial of this intervention.

42

Title: Association Between Early Prescribed Opioid Initiation and Risk of Suicidal Behavior **Presenter:** Fine, Kimberly

Authors: Kimberly Fine, PhD, Department of Applied Health Science, Indiana University, Bloomington; Martin E. Rickert, PhD, Department of Psychological and Brain Sciences, Indiana University, Bloomington; Lauren M. O'Reilly, BS, Department of Psychological and Brain Sciences, Indiana University, Bloomington; Ayesha C. Sujan, MA, Department of Psychological and Brain Sciences, Indiana University, Bloomington; Katja Boersma, PhD, Center for Health and Medical Psychology (CHAMP), School of Law, Psychology and Social Work, Örebro University, Örebro, Sweden; Zheng Chang, PhD, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden; Johan Franck, MD, PhD, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden; Paul Lichtenstein, PhD, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden; Henrik Larsson, PhD, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden; School of Medical Sciences, Örebro University, Örebro, Sweden; Brian M. D'Onofrio, PhD, Department of Psychological and Brain Sciences, Indiana University, Bloomington; Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden; Patrick D. Quinn, PhD, Department of Applied Health Science, School of Public Health, Indiana University, Bloomington

Abstract: Prescription opioid use has been linked to increased risk of suicidal behavior in adults. However, little research exists examining the role of prescription opioid use on risk of suicidal behavior in children and adolescents. This population is at high risk for suicidal behavior, as suicide is the second leading cause of death for people ages 10 to 34. Using healthcare data from Swedish population registers, we aimed to characterize the extent to which exposure to opioids at a young age leads to an increased risk of new onset suicidal behavior, for those with no history of suicidal behavior. Compared to demographically matched non-recipients, young people who initiated prescription opioids had just under three times the rate of subsequent suicidal behavior (HR = 2.64, 95% CI, 2.47-2.81). Compared to their unexposed siblings, young people who initiated prescription opioids had roughly two times the rate of subsequent suicidal behavior (HR = 1.83, 95% CI, 1.67-2.01). Finally, compared to young people initiating prescription NSAIDs, young people who initiated prescription opioids had only 19% relatively greater rates of suicidal behavior (HR, 1.19, 95% CI, 1.11-1.27). These results suggest the association between prescription opioids and suicidal behavior may be driven by the underlying pain indication.

43

Title: Circadian Rhythm Disruption Results in Visual Dysfunction Presenter: Mathew, Deepa Authors: Deepa Mathew and Ashay D Bhatwadekar, Department of Ophthalmology, Indiana

University School of Medicine, Indianapolis. IN 46202

Abstract: Circadian rhythm disruption (CRD) is associated with metabolic and neurodegenerative diseases. However, its effect on vision is poorly understood. The study aimed to assess the impact of CRD on retinal morphology, physiology, and vision, by exposing the mice to a shorter light-dark cycle (L10:D10) for 10 weeks. The L10:D10 mice exhibited three different circadian wheel running behaviors; 'entrained', 'free-running' and 'zigzagging'. At the end of 10 weeks, all L10:D10 behavioral groups exhibited reduced visual acuity and retinal thickness, and lesser number of photoreceptor cells. The entrained group had significantly reduced scotopic ERG a-wave and b-wave amplitudes, while the 'free-running' and 'zigzagging' groups showed normal ERG response. All L10:D10 behavioral groups exhibited specific differential retinal proteome and the entrained group had protein expression changes associated with retinal degeneration. Our results demonstrate that CRD resulted in photoreceptor degeneration and visual dysfunction. Our data uniquely show different circadian behaviors in response to L10:D10 cycle, and their specific effects on retinal physiology. Our data have broader implications in understanding the impact of circadian rhythm disruption on vision health, and possibly mitigating those impacts by behavior modifications.

44

Title: Silencing of the neuronal nitric oxide synthase gene in the basolateral amygdala impairs cued fear memory consolidation

Presenter: Patel, Jheel

Authors: Jheel Patel1,2,3, Erik T Dustrude2,3, Andrei I Molosh2,3, Anantha Shekhar1,2,3,4 1Medical Neuroscience Graduate Program; 2Paul and Carole Stark Neurosciences Research Institute; 3Department of Psychiatry, Indiana University School of Medicine, Indianapolis, IN;4Indiana Clinical and Translation Sciences Institute, Indiana University School of Medicine, Indianapolis, IN

Abstract: Fear and anxiety are evolutionarily developed responses to perceived or anticipated threats. Normal learning can produce avoidance behavior that promotes survival, but excessive and persistent fear after trauma can lead to development of phobias and post-traumatic stress disorder (PTSD). Involvement of the amygdala in fear acquisition is very well described and requires activation of N-methyl-D-aspartic acid receptors (NMDARs). At a cellular level, NMDAR activation leads to production of nitric oxide (NO) by a process that is mediated by interaction between postsynaptic density protein 95 (PSD95) and nitric oxide synthase (nNOS). To further understand the role of the PSD95-nNOS-NO pathway in cued fear, we utilized an adeno-associated virus mediated

knockdown of the nNos gene (or scrambled siRNA for control) in the basolateral amygdala (BLA) of Sprague-Dawley rats. We found no differences between control and nNos-knockdown rats in their locomotor activity, spatial memory, social interaction, anxiety-like behavior, and cued fear acquisition. However, cued fear consolidation was significantly attenuated in nNos-knockdown rats. Our results reveal that nNOS in the BLA is a novel genetic target underlying the mechanism of cued fear consolidation and can inform future therapeutic strategies for targeting fear and anxiety related disorders like PTSD.

<u>Acknowledgements</u>: This project was supported by the Indiana Clinical and Translational Sciences Institute funded, in part, by Grant Number TL1TR002531 from the National Institutes of Health, National Center for Advancing Translational Sciences, Clinical and Translational Sciences Award; by the Paul and Carole Stark Fellowship to JP; and R21 MH104018, MH052619 and R44 MH103936 to AS.

45

Title: Single-cell RNA-sequencing analysis of human inner ear organoids using AutoClustR: A computational tool for unbiased cell type discovery
Presenter: Romano, Daniel
Authors: Daniel R. Romano, Alex Solivais, Jing Nie, Eri Hashino

Abstract: Sensorineural hearing loss is the most common form of permanent hearing loss, which is itself among the most prevalent sensory impairments. While hearing aids and cochlear implants provide great benefit to many hearing-impaired individuals, they are not curative. More precise approaches will undoubtedly require a deeper understanding of developmental and pathological processes in the inner ear. Droplet-based single-cell RNA sequencing (scRNA-seq) has recently emerged as a powerful tool for dissecting these processes. Unsupervised clustering is a crucial step in scRNA-seq analysis, as cell clusters are presumed to correspond with distinct cell types, subtypes, and states. However, current clustering algorithms are driven by cluster number estimates, which are not readily available for potentially fruitful applications of scRNA-seq, such as the discovery of cell types and the validation, optimization, and comparison of stem cell differentiation protocols. To address this problem, we developed AutoClustR, an R-based computational tool for unbiased clustering of scRNA-seq data. Using seventeen datasets, we show that AutoClustR outperforms two similarly focused tools. Next, we used AutoClustR to reveal an unprecedented – and previously unappreciated – cellular diversity within stem cell-derived inner ear organoids. We envisage AutoClustR as invaluable to the ultimate development of cell-based and gene therapies for sensorineural hearing loss.

ONCOLOGY

46

Title: Simultaneous inhibition of p65 (NF-κB, ReIA) and PDK2 Increases Cytotoxicity and Radiationinduced Cell Killing of Pancreatic Adenocarcinoma

Presenter: Huang, Christina

Authors: Christina C. Huang MS1, Joseph Boone BS1, Mintare Cesiunaite2, Maria Vandevord2, Maria Khan BS1, Josh Streveler BS1, Ryan Erdwins BS1, Helen Chin-Sinex BS3, and Marc S. Mendonca PhD3, 4; 1Indiana University School of Medicine, Indianapolis, IN; 2Indiana University-Purdue University Indianapolis, Indianapolis, IN; 3Indiana University School of Medicine Department of Radiation Oncology, Indianapolis, IN; 4Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, IN 46032 USA.

Abstract: Background: High treatment resistance contributes to the low overall survival rates of patients with pancreatic ductal adenocarcinoma (PDAC). Cancer cell proliferation can be increased with upregulation of the NF-IB pro-cell survival pathway and by upregulation of the Warburg metabolism pathway, an alternative metabolic pathway that utilizes lactate rather than oxidative phosphorylation to outcompete normal cells. Dimethyl-amino-parthenolide (DMAPT) and dichloroacetate (DCA) are known inhibitors of p65 ReIA of the NF-2B signaling pathway and pyruvate dehydrogenase kinase (PDK-2), a regulator of Warburg metabolism, respectively. Methods: Established PDAC cell lines, MIA-PaCa-2, Panc-1, and AsPc-1, were treated a combination of DMAPT, DCA, sip65, and siPDK2 with and without radiation. Clonogenic survival assays, split dose repair experiments, and gamma-H2Ax immunofluorescence were performed. Results: We show that simultaneous treatment of PDAC cells with DMAPT and DCA in addition to siRNA directed at p65 and siRNA directed at PDK2 induces cytotoxicity and radiation-induced cell killing. Furthermore, using split dose experiments and gamma-H2Ax foci analysis, we show that treatment with DMAPT and DCA in PDAC cells inhibits double strand break repair. Conclusion: A dual approach using simultaneous chemical and genetic inhibition of NF-kB and Warburg metabolism may have therapeutic potential in the treatment of pancreatic cancer.

47

Title: Mesenchymal Breast Cancer Cells Modulate Extracellular Fibronectin Levels to Enhance Metastatic Outgrowth

Presenter: Libring, Sarah

Authors: Sarah Libring, Luis Solorio, Weldon School of Biomedical Engineering, Purdue University

Abstract: Breast cancer (BC) is the second leading cause of cancer deaths in women. Analysis of the Molecular Taxonomy of Breast Cancer International Consortium (METABRIC) dataset strongly links high levels of fibronectin (FN) expression to decreased patient survival. We found that autocrine FN stabilized a mesenchymal phenotype in BC cells. Tumors formed with a heterogenic mix of epithelial-like and mesenchymal-like BC cells increased the rate of metastatic outgrowth by the proliferative epithelial fraction when compared to homogeneous primary tumors. These mesenchymal BC cells secreted robust levels of soluble FN into the microenvironment. However, we establish that none of 15 tested BC cell lines were able to independently organize a FN matrix. Instead, BC cells manipulated the FN matrix production of fibroblasts in a phenotypic and signaling dependent manner. When full BC conditioned media was given to fibroblasts in a paracrine model,

epithelial-mesenchymal heterogeneity or plasticity resulted in the largest FN matrix production. In contrast, isolated extracellular vesicles from the homogeneous mesenchymal cells resulted in the most FN. These results support the idea that the mesenchymal BC fraction is necessary for the outgrowth of metastatic disease, in part, through their ability to modulate the FN concentration at primary and secondary sites.

48

Title: Radioluminescent nanoparticles for combination chemoradiotherapy of locally advanced head and neck cancers

Presenter: Sarkar, Kaustabh

Authors: Kaustabh Sarkar1, You-Yeon Won2; 1Graduate Research Assistant, Purdue University; 2Professor of Chemical Engineering, Purdue University

Abstract: Head and neck squamous cell carcinomas are the 8th most common cancers detected annually in the United States. A concurrent chemotherapy and radiotherapy ("chemoradiation") regimen is currently the standard of care for locally advanced head and neck tumors. However, chemoradiation causes several severe toxic side effects in a significant portion of the patient population. A formulation consisting of calcium tungstate nanoparticles encapsulated with polyethylene glycol-b-polylactic acid loaded with paclitaxel (PEG-PLA/CWO/PTX) has been developed to provide localized radiation triggered intratumoral chemoradiation. The drug release rate of PTX from the formulation can be controlled using radiation dose and frequency, a strategy that can be used to maintain a therapeutic concentration of drugs in the tumor for an extended period. The difference in stereochemistry of loaded PTX on the in vitro and in vivo efficacy of PEG-PLA/CWO/PTX formulation has been studied. The stereochemistry of PTX affects the in vitro release kinetics and causes significant differences in the in vivo efficacy of the formulation in mouse xenograft models. The differences in stereochemistry may not cause significant differences when used in free form but can significantly affect its performance when used within nanomedicine drug delivery carriers.

49

Title: ST2 as checkpoint target for colorectal cancer immunotherapy **Presenter:** Van der Jeught, Kevin

Authors: Kevin, Van der Jeught, Medical and Molecular Genetics, Indiana University School of Medicine; Yifan, Sun, Medical and Molecular Genetics, Indiana University School of Medicine; Zhuolong Zhou, Medical and Molecular Genetics, Indiana University School of Medicine; Thua, Jiang, Pediatrics, Indiana University School of Medicine; Jinfeng, Yang, Pediatrics, Indiana University School of Medicine; Jinfeng, Yang, Pediatrics, Indiana University School of Medicine; Malgorzata M., Kamocka, Medicine, Indiana University School of Medicine; Indiana University School of Medicine, Indiana University School of Medicine; Indiana University School of Medicine, Indiana University School of Medicine; Indiana University School of Medicine; Indiana University School of Medicine; Ka Man, So, Center for Computational Biology and Bioinformatics, Indiana University School of Medicine; Yujing, Li, Medical and Molecular Genetics, Indiana University School of Medicine; George E., Sandusky, Pathology and Laboratory Medicine, Indiana University School of Medical and Molecular Genetics, Indiana University School of Medicine; Michael, Frieden, Medical and Molecular Genetics, Indiana University School of Medicine; Michael, Frieden, Medical and Molecular Genetics, Indiana University School of Medicine; Michael, Frieden, Medical and Molecular Genetics, Indiana University School of Medicine; Michael, Frieden, Medical and Molecular Genetics, Indiana University School of Medicine; Michael, Frieden, Medical and Molecular Genetics, Indiana University School of Medicine; Harald, Braun, VIB Center for Inflammation Research and Biomedical Molecular Biology, Ghent University; Xiaoming, He, Bioengineering, University of Maryland; Xinna, Zhang, Medical and Molecular Genetics, Indiana University School of Medicine;

Chi, Zhang, Medical and Molecular Genetics, Indiana University School of Medicine; Sophie, Paczesny, Pediatrics, Indiana University School of Medicine; Xiongbin, Lu, Medical and Molecular Genetics, Indiana University School of Medicine.

Abstract: Immune checkpoint blockade immunotherapy delivers promising clinical results in colorectal cancer (CRC). However, only a fraction of cancer patients develop durable responses. The tumor microenvironment (TME) negatively impacts tumor immunity and subsequently the clinical outcomes. Therefore, there is a need to identify other checkpoint targets associated with the TME. Early onset factors secreted by stromal cells as well as tumor cells often help recruit immune cells to the TME, among which are alarmins such as interleukin-33 (IL-33). The only known receptor for IL-33 is STimulation 2 (ST2). Here we demonstrated that high ST2 expression is associated with poor survival and is correlated with low CD8+ T-cell cytotoxicity in CRC patients. ST2 is particularly expressed in tumor-associated macrophages (TAMs). In preclinical models of CRC, we demonstrated that ST2-expressing TAMs (ST2+TAMs) are recruited into the tumor via CXCR3 expression and exacerbate the immunosuppressive TME, and that combination of ST2 depletion using ST2-knock out mice, with anti-programmed death 1 treatment resulted in profound growth inhibition of CRC. Finally, using the IL-33trap fusion protein, we suppressed CRC tumor growth and decreased the tumor-infiltrating ST2+TAMs. Together, our findings suggest that ST2 could serve as a potential checkpoint target for CRC immunotherapy.

50

Title: Bilirubin-Coated Radio-Luminescent Particles for Radiation-Induced Photodynamic Therapy **Presenter:** Viswanath, Dhushyanth

Authors: Dhushyanth Viswanath, PI: Dr. You-Yeon Won

Abstract: Photodynamic therapy (PDT) has shown potential as a cancer treatment modality, but its clinical application is limited due to its visible light activation since visible wavelengths of light cannot penetrate tissues well. Additionally, combination therapies utilizing PDT and radiotherapy (RT) have shown clinical promise in several cancers but are limited again by light penetration and the need for selective photosensitization of the treatment area. We report the development of bilirubin-photodynamic nanoparticles (PEG-BR/CWO NPs). PEG-BR/CWO NPs are a formulation of PEGylated bilirubin micelles encapsulating CaWO4 nanoparticles. These particles are capable of activating PDT via X-ray irradiation within deep tissues due to the radio-luminescent properties of their CaWO4 nanoparticle cores. PEG-BR/CWO NPs facilitate a combination of PDT and radiation therapy and represent a previously unexplored application of PEG-bilirubin conjugates as a photosensitizing agent. When irradiated by X-rays, PEG-BR/CWO NPs emit UV-A and visible light from their CaWO4 cores which excites bilirubin and leads to the production of singlet oxygen. PEG-BR/CWO NPs exhibit improvements over X-ray therapy alone in in vitro and in murine xenograft models of head and neck cancer. The results of our studies indicate that PEG-BR/CWO NPs are promising agents for facilitating combined RT-PDT in deep-seated tumors.

RESEARCH CORES/CENTERS

Research Core/Center: 3D Bioprinting Core **Affiliation:** Indiana University School of Medicine **Director:** Lester Smith, PhD

Description:

We help users bioprint, perfuse, and oxygenate tissue models for their research. We have a workflow for semi-automated tissue bioprinting, manual tissue biofabrication, as well as several bioreactors (which fit in an incubator) for tissue cultures that provide controlled perfusion and full oxygenation.

Services:

- Consultation
- Spheroid microtissue scanning
- Bioprinting
- Tissue/perfusion/oxygenation culture
- Bioreactor design
- Training

Contact Information: Lester Smith (smitlej@iu.edu) 317-278-8057

Website: Click here

Research Core/Center: Biological Evaluation Affiliation: Purdue University Director: Bennett Elzey, PhD Manager: Sandra Torregrosa-Allen

Description:

The mission of the Biological Evaluation Shared Resource (BE-SR) is to provide expert guidance to investigators in grant preparation, model selection and experimental design, and to perform toxicity testing and proof-of-concept efficacy studies for the advancement of their projects using in vivo testing.

- Xenograft and Syngeneic models:
 - o Subcutaneous, intraperitoneal, intracardiac and intravenous Tumor Model Implantation
 - Orthotopic Tumor Models: Bladder, pancreas, prostate, kidney subrenal capsule, intracranial, breast fat pad,
- PDX models
- Efficacy Studies
 - Mouse weight
 - Tumor size monitored by caliper measurements for subcutaneous models and/or in vivo imaging for orthotopic or disseminated models
- In Vivo Hollow Fiber Model
- Toxicity Study, Maximum-Tolerated Dose (MTD) and Pharmacokinetic (PK) Studies
- Drug administration: intravenously (IV), intramuscularly (IM), intraperitonealy (IP), and subcutaneously (SC), Intratracheal instillation, by food and/or drinking water

- In Vivo Imaging studies:
 - IVIS Caliper bioluminescence and fluorescence
 - Micro CT
 - o Ultrasound
 - o Euthanasia, necropsy with organ and tissue collection
 - Blood draw including cardiac and retro-orbital
- PDX tumor maintenance and expansion
- Cell culture

Contact Information:	Bennett D Elzey (belzey@purdue.edu) 317-278-3449
	Sandra Torregrosa-Allen (storregr@purdue.edu) 765-496-0212

Website: Click Here

Research Co	bre/Center: Biospecimen Management Core Clinical and Translational Support
Lab/Specim	en Storage Facility (CTSL/SSF)
Affiliation:	IUPUI
Director:	CTSL – Christie Orschell, PhD
	SSF – Robert Orr
Manager:	CTSL – Robert Orr
	SSF – Jenna York

Description:

Our Biospecimen Management Core (BMC) offers cost-efficient processing & storage services with a focus on consistent quality and sample integrity.

The Specimen Storage Facility (SSF) currently maintains four mechanical freezer storage sites and a LN2 freezer storage site. Both investigator and SSF owned freezers are monitored and maintained by SSF staff 24/7 to virtually eliminate specimen loss due to freezer failures. Quality is maintained via our contracted independent QA oversight and guidance. Our facility and procedures are ISBER compliant (International Society for Biological and Environmental Repositories).

The Clinical and Translational Support Laboratory (CTSL) provides SOP-driven, protocol specific processing and shipping services for studies collecting human derived research specimens. The highest levels of quality and consistency are assured due to our voluntary compliance to GCPs and GLPs along with independent QA oversight.

- Specimen Processing
 - Sample Processing basic processing/preparation of samples for future analysis performed to protocol specific requirements.
 - DNA Extraction Services via manual method.
 - Shipping Services staff trained and certified for shipping exempt/Category B specimens (IATA/DOT/EHS compliant training).
 - Protocol Support and Setup including consultation, sample collection kit preparation, label design, and printing, etc.

- Storage
 - Short and Long Term Storage of Samples- mechanical freezers; liquid nitrogen
 - PI Owned Freezer Storage and Maintenance worry-free freezer monitoring and maintenance program.
 - LN2/Dry Ice Supply cost effective source for critical storage/shipping coolants.

Contact Information: Robert Orr CTSL Operations Manager (ctslab@iupui.edu) 317-944-9726 Jenna York - Storage Facility Manager (ictsissf@iupui.edu) 317-274-2213

Website: Click here

Research Core/Center: Biostatistics Consulting Center **Affiliation:** Indiana University Bloomington **Director:** Stephanie Dickinson

Description:

Biostatistical support is available through faculty collaboration or professional fee-for-service for study design and data analysis on health-related research projects.

Services:

- Study design & protocol development
- Grant development
- Sample size calculation & power analysis
- Data management
- Data analysis & modelling
- Manuscript preparation
- Public data sharing
- Review and verification of analyses

Contact Information: biostats@indiana.edu 812-856-9010

Website: Click here

Research Core/Center: Cell and Gene Therapy Manufacturing Affiliation: Indiana University School of Medicine Director: Emily Hopewell, PhD Bioprocess Development Director: Sreedhar Thirumala, PhD Cell Immunotherapy and Transduction Director: Vicki Graves Vector Production Director: Daniela Bischof, PhD

Description:

The Cell and Gene Therapy Manufacturing (CGTM) Facility collaborates with investigators through all phases of cell and gene therapy manufacturing, from pre-clinical design through treatment of patients. The facility is under the direction of Emily Hopewell, PhD, and comprises the Cell Immunotherapy and Transduction Facility (CIT), the Vector Production Facility (VPF), and the Bioprocess Development and

Cell Manufacturing Lab (BDL). Each section of the CGTM is led by a facility director and all areas share a common Quality Assurance team and a common Quality Management Plan. The goal of this facility is to provide Good Manufacturing Practices (GMP)-grade products in support of investigators and clinicians involved in Cell and Gene Therapy trials through 1) bioprocess development and technology transfer, 2) validation and manufacturing of vector and cellular products for use in clinical trials, and 3) clinical trial support.

Services:

- GLP Support
- Bioprocess Development
- Technology Transfer
- Large scale pre-clinical production
- GMP Services:
 - Vector Manufacturing: Retrovirus, Lentivirus, Cell banks, Clones
 - o Cell Manufacturing: Cell banks, autologous and allogeneic primary cell culture
 - Cell Immunotherapy and Transduction: genetic modification of primary cells, including hematopoietic progenitor cells and immune cells
 - Product release testing
- Regulatory support
- Product distribution and release

Contact Information: Emily Hopewell (emlhope@iu.edu)

Website: Click here

Research Core/Center: Center for Genomics and Bioinformatics **Affiliation:** Indiana University Bloomington (Office of the Vice Provost for Research)

Director: Matthew Hahn, PhD

Description:

The CGB offers a wide range of genomic services, including high-throughput DNA/RNA extraction, library preparation, next-generation sequencing, and bioinformatic analysis. We also provide support in the early stages of projects, including consulting on experimental design, providing cost estimates, and writing letters of support for research proposals. We support an extremely diverse clientele, including researchers interested in human health, ecology, evolution, virology, microbiology, plant sciences, etc. Our goal is to facilitate high-quality cutting-edge research, while minimizing costs. The CGB's mission is to:

- Act as a service facility that provides IU faculty access to genome technologies and bioinformatic support.
- Provide consulting and training that supports the development of genome-enabled research programs and grant proposals.
- Develop new genome technologies and bioinformatics tools that are not easily purchased as a fee for service elsewhere.

- High-throughput DNA/RNA extraction
- Library preparation

- Next-generation sequencing
- Bioinformatic analysis

Contact Information: Rolf Rockliff (Fiscal Officer) (cgbadmin@iu.edu) 812-855-6877

Website: Click here

Research Core/Center: Center for Integrative Study of Animal Behavior (CISAB) Mechanism of Behavior Core Facility Affiliation: Indiana University Bloomington Director: David Sinkiewicz

Description:

The Mechanisms of Behavior core lab provides equipment and reagents for performing experiments on a molecular level. The director is also available for consultation on experimental design and introduction to molecular techniques.

Services:

- Shared use equipment, including:
 - o Quantitative Thermal Cycler
 - Standard Thermal Cyclers
 - o Maxwell RSC Automated Nucleic Acid Extraction
 - Microplate Spectrophotometer
 - Microplate Shaker
 - Analytical Balance
- Experimental Design Molecular approaches
- Equipment/Technique Training

Contact Information: David Sinkiewicz (dasink@iu.edu) 812-856-1139

Website: Click here

Research Core/Center: Center for Survey Research (CSR) Affiliation: Indiana University Bloomington Core Director: Ashley Clark Director, Research Project Management Services: Erica Moore Director, Research Data Management Services: Jamie Roberts Director, Research Technologies: Joe Wilkerson Director, R&D and Research Laboratory & Senior Methodologist: Lilian Yahng Director, Research Field Operations: Karen Tucker

Description:

Since the early 1980's, the Center for Survey Research has conducted thousands of quantitative and qualitative research projects, using surveys, interviews, focus groups, and a wide range of other methods. Our work advances knowledge and humankind by helping researchers plan for, gather, and analyze data in the medical and health sciences.

Our partners include collaborators from universities, governmental agencies, nonprofits, and businesses. We manage studies from start to finish—or support a discrete task like reviewing a questionnaire or conducting interviews.

Services:

- Support for developing research designs and proposals (using methods such as surveys, interviews, focus groups, etc.)
- Instrument design and testing, including cognitive interviewing
- Database and data collection instrument programming, including REDCap and Qualtrics
- Sampling and subject recruitment
- Quantitative data collection (in person, online, mail, and telephone) and qualitative data collection (focus groups, semi-structured interviews, observations, etc.)
- Standardized collection of medical specimens (including saliva, blood, and urine) and anthropometric measurements
- Forms scanning, data entry, and coding
- Data processing and analysis, including weighting
- Custom training for research teams (e.g., best practices for cognitive interviewing)
- Consultations and workshops

Contact Information: Web contact and appointments form: csr.indiana.edu/contact us Phone: 812-856-0779 or toll-free 800-258-7691

Website: Click here

Research Core/Center: Chemical Genomics Core Facility Affiliation: Indiana University School of Medicine Director: Michael Weiss, MD, PhD, MBA Director of Chemistry and Informatics: Lifan Zeng, PhD Director of High-Throughput Screening: Jingwei Meng, PhD

Description:

The Chemical Genomics Core Facility (CGCF) at the Indiana University School of Medicine seeks to provide sophisticated small molecule informatics, design and synthesis; to facilitate faculty-driven high-throughput screening and high-content analysis; and to perform small and large molecule analysis for academic and industrial investigators.

The CGCF locates in the Van Nuys Medical Science Building in Indianapolis. The core is equipped with five hoods for chemical synthesis, a microwave reactor, a parallel synthesizer and preparative HPLCs; a collection of 227,680 diversified small molecules, liquid handling and assay detection systems; and analytical instruments such as LC-QTOF and NMR.

- Cheminformatics on small molecule information retrieval, recommendation, and physicochemical property evaluation.
- High Throughput Screening on assay development for small molecules.
- Medicinal Chemistry on design and synthesis of small molecules and peptides as inhibitors, probes & activators.

- High Content Analysis on cell imaging-based applications.
- Analytical Chemistry on LC-QTOF and NMR analysis of small molecules, peptides, and large molecules, such as nucleotides, and proteins.

Contact Information:	Michael Weiss (weissma@iu.edu)
	Jingwei Meng (mengj@iu.edu)
	Lifan Zeng (zengl@iu.edu)

Website: Click here

Research Core/Center: Chemical Genomics Facility Affiliation: Purdue University Director: Zhong-Yin Zhang, PhD Manager: Lan Chen

Description:

The Chemical Genomics Facility (CGF) is an official CTSI core that is affiliated with Purdue Institute for Drug Discovery. We provide expertise and resources for investigators from Purdue and other institutions to access to the state-of-art technologies and instrumentation enabling high-throughput approaches (HTS and HCS) for functional genomics and chemical biology studies to facilitate drug discovery. Our experienced facility staff work closely with each investigator and provide services through all stages of the lead discovery process, including consultation, assay implementation, chemical libraries, screen automation and data processing. We also provide instruments that helps with hit validation using various biophysical approaches. The facility is designed to be highly flexible in order to meet the needs of multiple users employing a range of assays from a wide range of disciplines.

Services:

- Assay implementation and optimization of various biochemical assays of enzyme activity, protein-protein interaction and cell-based reporter gene assays and phenotypic assays
- Chemical libraries of over 500,000 compounds categorized into diversity-based, targeted, natural products, known drugs, bioactives, fragments libraries
- siRNA libraries of human kinase and phosphatase, and arrayed human genome CRISPR library
- Robotic equipment such as liquid handling workstations, dispensers, plate readers, high content imaging system etc.
- Hit validation using Isothermal Titration Calorimetry (ITC), MicroScale thermophoresis (MST), thermal shift assay (TSA), and Functional Drug Screen System (FDSS) mCell for ion channel, GPCR Ca2+ assays

Contact Information: Zhong-Yin Zhang, (zhang-zy@purdue.edu) Lan Chen, (lanchen@purdue.edu)

Website: Click here

Research Core/Center: Clinical Pharmacology Analytical Core Affiliation: Indiana University School of Medicine/Indiana University Simon Cancer Center Core Director: Andi Masters, MS Scientific Director: Zeruesenay Desta, PhD

Description:

Detailed understanding of drug disposition and factors affecting this process is important to guide preclinical drug discovery and development and in optimizing available drug therapies. CPAC specifically focuses on providing scientific and technical services to help investigators in their preclinical and clinical drug metabolism and pharmacokinetic studies. To support these activities, CPAC utilizes state-of-the-art LC-MS/MS methods to quantify small molecules (drugs, metabolites, and new chemical entities) from a wide variety of biological samples (plasma, urine, tissues, media, etc.). CPAC provides investigators with detailed information on in vivo pharmacokinetics (PK), drug interactions, in vitro drug metabolic stability, formulation optimization, protein binding, drug purity verification, and drug stability. CPAC is the only analytical core on campus that offers a unique combination of extensive expertise on in vitro and in vivo drug metabolism, including stereoselective metabolism, drug-drug interactions, and pharmacokinetics (PK).

Services:

- Method development to quantify small molecules (drugs, metabolites, and new chemical entities) from a wide range of biological matrices utilizing HPLC-MS/MS
- Drug purity verification and stability
- In vitro metabolic stability
- Formulation solubility and stability
- Protein binding
- In vivo pharmacokinetics
- Non compartmental analysis

Contact Information: Andi Masters (argrove@iu.edu)

Website: Click here

Research Core/Center: Electron Microscopy Center Affiliation: Indiana University School of Medicine Director: Monte Willis, MD, PhD, Indiana Center for Musculoskeletal Health Assistant Director/Lab Manager: Caroline Miller

Description:

The Indiana University School of Medicine Electron Microscopy Center is a full-service research laboratory providing both Transmission and Scanning Electron Microscopy. The center can provide the technical services to help design and then implement experiments needing either type of microscopy. Free consultation with assistant director/lab manager is provided with any new experiment. The service provided can apply both traditional methods and more recent technical developments to suit the investigator's needs.

Services:

- Transmission Electron Microscopy (TEM). ThermoFisher, Tecnai, Spirit, (Hillsboro, OR) equipped with an AMT (Advanced Microscopy Techniques, Danvers, MA) CCD camera. Routine processing of specimens, fixation through embedding. Thick and thin sectioning with staining. Viewing and imaging on microscope. Various specimen types accepted, from tissue pieces to cell cultures either as a monolayer or cell pellet. Negative staining can be done on various specimens, such as virus, bacteria, exosomes or even hallosite crystals in clay.
- Immunocytochemistry. This would include processing of specimens with a special fixative and embedding resin used for immunostaining, thick and thin sectioning, the immunostaining process, primary antibody provided by the researcher, secondary antibody provided by the EM Center. Viewing and imaging on the microscope.
- Scanning Electron Microscopy (SEM). JEOL 6390 LV (Peabody, MA). Routine processing of specimens with fixation, chemical drying, mounting, and sputter-coating. Viewing and imaging on the scope.

Contact Information: Caroline Miller, (caromill@iupui.edu)

Website: Click here

Research Core/Center: Engineering MRI Facility Affiliation: Purdue University Director: Vitaliy Rayz, PhD Manager: Greg Tamer, PhD

Description:

The Engineering MRI Facility on Purdue's campus in PMRI provides a GE 3T MRI system for Purdue users and external users to employ for their MRI needs. Personnel are available to assist with experiment planning, implementation, scanning, and analysis.

Services:

- GE 3T MRI system with coils
- AV system
- Feedback system
- Anesthesia system
- MR-compatible NIRS system

Contact Information: Greg Tamer (gtamer@purdue.edu) 765-588-7134

Website: Click here

Research Core/Center: Flow Cytometry and Cell Separation Core Facility **Affiliation:** Purdue University **Director:** Jill E. Hutchcroft, PhD

Description:

The Flow Cytometry and Cell Separation Core Facility provides a variety of flow cytometry and single-cell genomics services, including cell sorting, flow cytometry analysis, individualized training, data analysis, experimental design, preparation of data and figures for publications and grants, and expert consultation and assistance. Available instrumentation includes two flow cytometry analyzers (BD Fortessa, Attune Nxt), three cell sorters in BSL-2 hoods (two BD Arias, one BC Astrios), and two systems for single cell genome and transcriptome analysis (10x Genomics, Fluidigm).

Services:

- Flow Cytometry Analysis
- Cell Sorting
- Single Cell Genome and Transcriptome analysis
- Expertise, Training, and Data Analysis, including experimental design, sample preparation, instrument usage and maintenance, data analysis, and preparation of grants and manuscripts.

Contact Information: Jill E. Hutchcroft (jehutchc@purdue.edu)

Website: Click here

Research Core/Center: Flow Cytometry Core Facility (IUB FCCF) Affiliation: Indiana University Bloomington Director: John Foley, PhD Assistant Director: Kris Klueg, PhD Manager: Christiane Hassel, MS

Description:

The IUB FCCF offers state-of-the-art flow cytometry analysis and cell sorting services for both the Indiana University Bloomington and broader scientific community. Flow cytometry allows researchers to analyze single cells or particles based on fluorescence and light scattering characteristics. Not only can the facility assist in analysis experiments, it can also assist with retrieving specific cell populations of interest. The facility is able to work with a wide variety of samples, ranging from sub-micron bacteria to large mammalian cells. The facility is also able to detect and sort larger particles including pollen, *C. elegans* worms, and *Drosophila* embryos. The facility also offers consultation services and access to data analysis software. Please contact the facility for additional information.

- Flow Cytometry Sorting
 - o BD FACSAria II
 - o Sony SH800
 - Union Biometrica COPAS Select
 - Flow Cytometry Analysis
 - o BD LSRII

- Miltenyi MACSQuant
- Cell counting Beckman Coulter Z2
 - Access to data analysis software
 - o FlowJo
 - FCS Express

Contact Information: Christiane Hassel (chassel@indiana.edu) 812-855-7101 1001 E 3rd Street Jordan Hall 029, Bloomington, IN 47405

Website: Click here

Research Core/Center: Flow Cytometry Resource Facility (FCRF) Affiliation: Indiana University School of Medicine Director: Baohua Zhou, PhD Manager: Andy Canciamille

Description:

The Flow Cytometry Resource Facility (FCRF) provides flow cytometric analysis and cell sorting services as well as flow cytometric image analysis and single cell genomics and proteomics (CyTOF) analyses. FCRF offers consultation, technical advice, experimental design assistance, and data interpretation services to promote use of state-of-the-art technologies and cutting-edge science. Four full-time employees who are well-qualified operators with extensive training and experience provide these services. The FCRF houses 3 flow cytometric analyzers and 3 sorters (up to 18 parameters), an image stream analyzer, and a CyTOF2.

Services:

- Multiparameter (up to 16 colors) immunofluorescence analysis and cell sorting
- CyTOF2 Mass Cytometer
- Multispectral Imaging Flow Cytometer
- DNA content and cell cycle analysis
- Apoptosis analysis (Annexin V/PI, Caspase, TUNEL and other assays)
- Chromosome analysis (univariate and bivariate)
- Receptor-ligand interactions
- Kinetic analyses
- Off-line data analysis
- Consultation to assist in study design and optimization

Contact Information: Andy Canciamille (acancia@iu.edu) 317-274-7587

Website: Click here

Research Core/Center: Freimann Life Science Center Affiliation: University of Notre Dame Director: Satish Adusumilli, DVM

Description:

The Freimann Life Science Center is home to virtually all laboratory animals supporting Notre Dame teaching and research. The FLSC primarily serves faculty from the Departments of Biological Sciences, Chemistry and Biochemistry, Chemical Engineering, and the Indiana University School of Medicine – South Bend.

Services:

- Procurement
- Animal care
- Breeding
- Training
- Limited procedures for research

Contact Information: Satish Adusumilli (freimann@nd.edu)

Website: Click here

Research Core/Center: Genomics & Bioinformatics Core Facility Affiliation: University of Notre Dame Director: Michael Pfrender, PhD Manager: Melissa Stephens

Description:

The Genomics & Bioinformatics Core Facility (GBCF) at the University of Notre Dame offers comprehensive services and support for state-of-the-art genomics experiments and bioinformatics analysis.

GBCF services are designed to provide genomics solutions and acquire data for a broad range of applications including metagenomics, cancer genomics, microbial genomics, non-model system genomics, transcriptomics, and epigenomics. The GBCF offers support for a diverse research community that spans basic biomedical research in human disease, vector disease research (arthropod vectors and parasites), population genomics, and environmental genomics. Custom and specialty workflows are welcome.

Our computing facilities are equipped with high performance hardware and computational resources. The Bioinformatics team offers services for standard and custom genomics analysis, data management, bioinformatics tool development, and access to biocomputing resources. Consultation is encouraged to guide experimental design, and to provide assistance in identifying appropriate technology for specific research needs.

- Illumina RNA/DNA NGS library construction
- Illumina MiSeq sequencing
- Illumina NextSeq sequencing
- 10X Genomics single cell library construction and sequencing

- ABI3730XL Sanger sequencing and fragment analysis
- RNA/DNA quality control
- Covaris S220 high-intensity acoustic shearing
- Sage Science BluePippin automated size selection
- Bioinformatics analysis
- Custom and specialty NGS workflows

Contact Information: Melissa Stephens (stephens.49@nd.edu) 574-631-0338

Website: Click here

Research Core/Center: HANDS Core

Affiliation: Indiana University School of Medicine Director: Naomi Swiezy, PhD, HSPP Co-Director: Tiffany Neal, PhD

Description:

The HANDS in Autism[®] Interdisciplinary Training & Resource Center is located within the Department of Psychiatry at the Indiana University School of Medicine. The HANDS Core is deeply integrated and involved statewide in providing evidence-based services, training, coaching and consultation across a range of local community and state stakeholder networks (e.g., families, medical providers, school personnel, community organizations). This involvement and integration in addressing the behavioral, educational, and vocational needs of consumers across a range of ages, functioning and disability types has assisted in (1) providing consultative expertise related to assessment and intervention with autism spectrum disorder (ASD) and related developmental (e.g., developmental and/or intellectual disabilities (DD/ID)) or neurodevelopmental disorders, (2) reaching an extensive audience for recruitment efforts, and (3) facilitating efforts related to community-based mixed methods, clinical trials and other research endeavors (e.g., survey development and dissemination, behavioral assessment and intervention) related to individuals with ASD/DD/ID across the lifespan.

Services:

The HANDS team offers a number of services relevant to the research missions of investigators through the HANDS Core including but not limited the following:

- Reaching an extensive audience for recruitment
- Conducting and/or guiding behavioral, educational, functional, and/or vocational assessments
- Assisting program evaluation efforts targeted to a range of community stakeholders
- Broadening community and research profiles and activities across participant groups
- Sharing data and information related to extensive literature and statewide gap analyses related
- Sharing and/or adapting of internally derived measures ranging in scope from gap analyses to knowledge and implementation of ABA-based interventions
- Facilitating implementation science efforts to guide programming as well as mixed methods and other research designs
- Consulting related to specialty content areas of: applied behavior analysis (ABA); special education; autism spectrum disorder (ASD) and other disabilities (e.g., ID/DD); implementation science and practice in the community; caregiver, teacher, and provider skills training

Website: Click here

Research Core/Center: Histology and Histomorphometry (HHC) Affiliation: Indiana University School of Medicine Director: Lilian I. Plotkin, PhD Manager: Drew M. Brown

Description:

The Histology Core provides histological services histomorphometric analysis for basic science (nonclinical) research. Both mineralized (plastic embedded) and soft tissue (paraffin embedded, and frozen) specimens can be prepared by the facility. In addition, image collection and dynamic and static bone histomorphometric measurements are offered by the core. The histology and histomorphometry laboratory offers a cost-effective approach to complete tissue processing and staining, as well as image collection and analyses, and the support from experienced personnel to multiple investigators from different institutions across the state and elsewhere in the United States. One hundred percent of the core resources are available to investigators on a fee for service basis. The core employs two full time and a part time histotechnicians, who are available for investigators consultation, training and tissue processing.

Services:

- Tissue embedding and sectioning (including methylmetacrilate mineralized bone embedding, paraffin embedding of demineralized bone and other tissues, and cryosections)
- Staining (H&E, special stains)
- Immunohistochemistry
- Dynamic and static bone histomorphometry
- Bone microdamage assessment
- Image collection and analysis

Contact Information: Drew M. Brown (drebrown@iupui.edu) 317-274-7558

Website: Click here

Research Core/Center: Indiana Institute for Biomedical Imaging Sciences (IIBIS) In-Vivo Imaging Core Affiliation: Indiana University School of Medicine Directors: Gary Hutchins, PhD; Yu-Chien Wu, MD, PhD; Scott Snyder, PhD Managers: Jason Shine, Jieun Kim, PhD

Description:

The Indiana Institute for Biomedical Imaging Sciences (IIBIS) financially supports and maintains an In-Vivo Imaging Core as a service provider and research center for imaging and radiotracer development. We provide imaging services for clinical trials, observational and preclinical studies, and radiochemistry support for molecular imaging. Currently, the Core is equipped with state-of-the-art imaging systems, including a Siemens 3.0T PrismaFit magnetic resonance imaging (MRI) scanner, a Siemens 3.0T Prisma MRI scanner, a Siemens Vision positron emission tomography (PET) - computer tomography (CT) scanner, a Siemens Biography PET-CT scanner, an in-house-built PET scanner, a Bruker 9.4 T PET-MRI scanner, a Siemens Eclipse Medical Cyclotron, and Radiochemistry Facilities. In addition, highly skilled faculty and staff are available to assist with research study design, and image data collection, processing and analysis. We envision that personalized patient care will be facilitated by imaging-driven diagnosis of disease, imaging-guided therapy, and imaging-based assessment of treatment response.

Services:

- Experimental Design
- PET
- MRI
- Animal handling
- Radiotracer development and production
- Imaging technique development
- Proposal preparation
- Budget planning
- Data analysis
- Manuscript preparation

Contact Information: Jason R. Shine (jrshine@iupui.edu) Jieun Kim (jk147@iu.edu) Scott E Snyder (ssnyder7@iu.edu)

Website: Click here

Research Core/Center: Indiana University Nuclear Magnetic Resonance Facility (NMR) Affiliation: Indiana University Bloomington Director: Xinfeng (Frank) Gao, PhD

Description:

Indiana University Nuclear Magnetic Resonance (NMR) facility provides access to state-of-the-art instrumentation and expertise in solution NMR spectroscopy. The facility has six high resolution NMR spectrometers from 400 MHz to 800 MHz to perform all modern solution-state experiments for structural elucidation, molecular dynamics and reaction kinetic study of small molecules and large biological molecules in solution.

Services:

- 1D and 2D solution state NMR experiments.
- Multi-nuclear NMR measurements.
- Multi-dimensional NMR experiments for large biological molecules in solution.

Contact Information: Frank Gao (xgao@indiana.edu) 812-855-6492

Website: <u>Click here</u>

Research Core/Center: Indiana University Simon Comprehensive Cancer Center Tissue Procurement and Distribution Core (IUSCCC) Affiliation: Indiana University School of Medicine Associate Director for Clinical Research: Kathy Miller, MD Core Director: Oscar Cummings, MD Operations Manager: Mary Cox

Description:

The IUSCCC Tissue Procurement and Distribution Core collects, processes and stores surgical tissue, blood and bone marrow aspirate from patients with cancer to be used by researchers for the examination of relevant cellular and molecular properties in preclinical drug development assays. The core contains cancer samples, cancer samples with normal and normal adjacent controls and a limited amount of normal samples. To request services and samples from the core, complete a sample request form which can be found at www.cancer.iu.edu/tissue. A price list is also available under the Services tab. All requests are reviewed for scientific merit and content.

Services:

- Collection and storage of human specimens from multiple IU Health hospital sites
- Distribution of fresh, frozen and formalin-fixed paraffin-embedded tissue
- Distribution of whole blood, plasma, serum and cellular (MNC/DNA) components
- Distribution of bone marrow aspirate and core biopsies
- Slide preparation: H&E stained or unstained
- Tissue microarray preparation
- Collection of defined clinical information
- Assistance with approved PI initiated sample collections
- Retrieve and distribute archived tissue requests for interventional clinical trials

Contact Information: Mary Cox (marmacox@iupui.edu) 317-274-4320

Website: Click here

Research Core/Center: Infectious Diseases Laboratory (IDL) Affiliation: Indiana University School of Medicine Director: Aaron Ermel, MD Manager: Jim Williams

Description:

The Infectious Diseases Laboratory (IDL) is a Core Laboratory Facility for the Indiana Clinical and Translational Sciences Institute (CTSI). The IDL is skilled in performing clinical research studies including the evaluation of new technologies for the diagnosis of sexually transmitted pathogens, developing novel assays to meet the needs of individual research collaborators, and tailoring services to successfully meet study objectives. Many of the assays evaluated by our laboratory have become standard diagnostic techniques. Available molecular testing includes Chlamydia trachomatis, Neisseria gonorrhoeae, Trichomonas vaginalis, Human Papillomavirus (HPV), Herpes Simplex Virus 1 and 2, and Mycoplasma genitalium. Routine specimen types include urine, vaginal, endocervical, oral, rectal, and liquid cytology medium. Culture isolation is available upon request for Chlamydia trachomatis, Neisseria gonorrhoeae, and Trichomonas vaginalis. In addition to the main laboratory, an adjacent laboratory provides sophisticated diagnostic services specifically focused on HPV including molecular typing.

Services:

- Assay Development
- Chlamydia trachomatis nucleic acid amplification assay and cell culture
- Neisseria gonorrhoeae nucleic acid amplification assay and cell culture
- Trichomonas vaginalis nucleic acid amplification assay and cell culture
- Human Papillomavirus nucleic acid amplification assay and molecular typing
- Herpes Simplex Virus 1 and 2 nucleic acid amplification assay
- Mycoplasma genitalium nucleic acid amplification assay
- Specimen Logistics Handling
- Biorepository

Contact Information: Email: idl@iu.edu 317-274-1422

Website: Click here

Research Core/Center: Integrated Imaging Facility (NDIIF) Affiliation: University of Notre Dame Director: Bradley D. Smith, PhD Manager: Sarah Chapman

Description:

The Notre Dame Integrated Imaging Facility (NDIIF) is a state-of-the-art research core that makes available to the Notre Dame science and engineering community, as well as external customers, an integrated suite of sophisticated microscopes and imaging stations. The NDIIF also provides resident professional staff (three Ph.D.-level imaging specialists and two technicians) to guide the non-expert users. The technical staff of the NDIIF are physically located with the instrumentation at three sites on the campus of the University of Notre Dame: basement of Stinson-Remick Hall (emphasis on electron microscopy), basement in Galvin Life Sciences (emphasis on optical microscopy and in vivo imaging), and Freimann Life Sciences Center (histology).

- Field Emission Scanning Electron Microscope (FEI, Magellan)
- Dual Source Focused Ion Beam (FEI, Helios G4)
- Transmission Electron Microscopes (FEI, Titan, JEOL 2011)
- Confocal Microscope (Leica)
- Deconvolution Fluorescence Microscope (Deltavision)
- One and Two-photon Confocal Microscope (Nikon A1R)
- C2 + Laser Scanning Confocal Microscope
- Advanced Molecular Imaging HT Instrument
- MARS Medipix Spectral X-ray CT
- Echo MRI

Contact Information: Notre Dame Integrated Imaging Facility 340 McCourtney Hall, Notre Dame, IN 46556 574-631-8251

Website: Click here

Research Core/Center: Indiana University Bloomington Electron Microscopy Center Affiliation: Indiana University Bloomington Director: Roger Innes, PhD Manager: David Morgan, PhD

Description:

The Indiana University Bloomington Electron Microscopy Center (IUB-EMC) provides equipment, services, and expertise for both biological and materials science electron microscopy. Our facility can be used on either a fee-for-use basis (where users pay for time on any of the equipment) or a fee-for-service basis (where users pay for staff members' time and for equipment time). We provide consultations at no cost and are happy to provide letters of support for proposals and grants of any sort.

Services:

Our equipment includes a 300 kV JEOL (S)TEM instrument, a 200 kV Thermo Talos Artica TEM, two lower voltage JEOL TEM's, a Thermo Teneo VolumeScope SEM and sample preparation equipment for TEM and SEM (including a Wohlwend high pressure freezing system and a Leica freeze substitution device). The 300 kV instrument is suitable for cryoEM and is equipped with a direct electron detecting camera from Direct Electron and an EDS detector from Oxford Instruments. The 200 kV instrument is a dedicated cryoTEM and equipped with two direct electron detecting cameras (a Falcon 3 from Thermo and a K3 from Gatan). Two of our staff have expertise in cryoEM.

Contact Information: David Morgan (dagmorga@indiana.edu) 812-856-1457 iubemc@indiana.edu Roger Innes (rinnes@indiana.edu) 812-855-2219

Website: Click here

Research Core/Center: Indiana University Simon Comprehensive Cancer Center In Vivo Therapeutics Core (IUSCCC) Affiliation: Indiana University School of Medicine Director: Karen E. Pollok, PhD Manager: Tony Sinn

Description:

The IUSCCC In Vivo Therapeutics Core (IVT) provides investigators with cost-effective and comprehensive services to facilitate the development and testing of novel pharmacological & cellular therapies. The Core will act as a liaison between the Principal Investigator and any other outcome analyses from live-phase studies. The IVT Core also maintains multiple on-site mouse breeding colonies, as well as oversees operation of the cesium irradiator facility.

Services:

- In Vivo Tumor Growth Kinetics Established lines include: SKOV-3X, & A2780 (Ovarian), A549, H460, & H1975 (Lung), MCF-7, TMD-231, MDA-MB-468, & BT474 (Breast), C32 (Melanoma), H929 & MM1S (Multiple Myeloma), Raji & Granta 519 (NHL), PaCa-2, ASPC-1, Panc-1 (Pancreatic), CHLA-9, CHLA-10, TC-71 (Ewing Sarcoma)
- PDX model development
- Pharmacological Investigations: In vitro toxicity testing utilizing primary human hematopoietic cells and clonogenic progenitor assays to test effects of new compounds on normal cellular function.
- In Vivo Dose Range Finding: Develop a rational dosing regimen for testing efficacy of therapy
- In Vivo Drug Efficacy/Tumor Xenograft Model: Establish tumors and administer drug regimen
- Cellular Therapies: Irradiation of mice prior to transplantation, Intravenous injection of hematopoietic stem cells

Contact Information: Tony Sinn, Core Manager, *In Vivo* Therapeutics (alsinn@iupui.edu) Indiana University Melvin and Bren Simon Comprehensive Cancer Center 1044 W. Walnut St. (R4, Room 324) Indianapolis, IN 46202-5188 317-274-8811

Website: Click here

Research Core/Center: Laboratory Animal Resource Center **Affiliation:** Indiana University School of Medicine **Director:** Deb Hickman, DVM, MS, DACLAM, DACAW

Description:

The Laboratory Animal Resource Center (LARC) contributes to and enhances the services and collaborative efforts of medical research at Indiana University School of Medicine. In addition to the provision of basic husbandry for a wide variety of laboratory animal species, the veterinary staff and other highly experienced laboratory animal professionals of the Indiana University School of Medicine LARC provide training, supplies, and specialized service support for medical research.

Mission:

At the Laboratory Animal Resource Center (LARC), we are dedicated to providing exceptional animal care which exceeds the needs of Indiana University School of Medicine and its research staff.

Vision:

Our vision is top-quality animal care and PI service provided by inspired and valued employees. The field of laboratory animal science has evolved substantially over the past two decades. We understand how the laboratory environment can both positively and negatively affect the results of research projects, and we recognize that an educated and empowered animal care team can be effective in working as an unofficial but critical member of the research team utilizing animal models. The LARC staff has deep experience in laboratory animal care and has achieved various levels of certification in laboratory animal science.

Services:

- Breeding Colony Management
- Technical Service Support
- Skills and Technique Training
- IACUC Protocol consultation
- Animal ordering
- Animal import and export

Contact Information: larc@iupui.edu, Phone: 317-274-8649, Fax: 317-274-1969

Website: Click here

Research Core/Center: Magnetic Resonance Research Center Affiliation: University of Notre Dame Director – Academic: Jeffrey Peng, PhD Director – Operations: Evgenii Kovrigin, PhD

Description:

The Magnetic Resonance Research Center supports research in chemistry, biochemistry, molecular biology, chemical engineering, and related fields. The Center operates eight different nuclear magnetic resonance spectrometers for liquids analysis ranging in magnetic field strength from 7 to 18.8 Tesla (300 to 800 MHz in proton frequency)

Services:

• Solution and solid-state NMR spectroscopy

Contact Information: Evgenii Kovrigin (ekovrigu@nd.edu) 574-631-8359

Website: Click here

Research Core/Center: Metabolite Profiling Facility Affiliation: Purdue University Director: Bruce Cooper, PhD Manager: Amber Jannasch

Description:

Metabolite profiling is an integral component of systems biology, an exciting field that combines genomics, transcriptomics and proteomics to define cellular functionality. The Metabolite Profiling Facility provides state-of-the-art technologies that enable both qualitative (defining all components of a metabolome) and quantitative (determining differential concentrations of metabolites) metabolomics in complex biological systems. This facility employs highly sensitive mass spectrometry coupled with liquid chromatography and gas chromatography for precise sample analysis. Our scientists empower researchers with new technologies, methods development, sample analysis, expert training, and consultation

Services:

• Targeted metabolomics

- Non-targeted metabolite profiling
- High-throughput lipid profiling
- Sample preparation
- Bioinformatics consultation
- Individual training
- Consulting and study design

Contact Information: bbcmpf@purdue.edu

Website: Click here

Research Core/Center: Multiplex Analysis Core Affiliation: Indiana University School of Medicine Director: Christie M. Orschell, PhD Manager: P. Artur Plett, PhD

Description:

The Multiplex Analysis Core (MAC) offers microplate-based immunoassay systems that can perform multiplex analysis of multiple different analytes in a single sample. The MAC uses a Bio-Plex 200 Multiplex System with High Throughput Fluidics based on Luminex technology. Commercially available Luminex-compatible kits are available to detect analytes such as cytokines, chemokines, hormones, cell signaling molecules, phosphoproteins or nucleic acids for a variety of animal species including human, mouse, cow, dog, pig, rat and primate. Custom kits are also a possibility. Samples such as sera, plasma, cell culture media, cell lysates, urine, and synovial fluid have been successfully analyzed in this facility and many analytes are detectable in the nanogram or picogram range. The MAC provides all reagents & buffers required to run the samples (excluding kits), analysis of raw data and optimization of standard curves using vendor software, and delivery of data to the user in an Excel spreadsheet.

Services:

• Microplate-based immunoassay multiplex analyses

Contact Information:	Artur Plett (pplett@iu.edu) 317-278-2485
	Hailin Feng (hfeng@iu.edu) 317-278-2485

Website: Click here

Research Core/Center: Purdue Genomics Facility **Affiliation:** Purdue University **Director:** Phillip San Miguel, PhD

Description:

The Genomics Facility provides gene sequencing services to researchers, including quality control and library preparation, as well as next generation MiSeq services, and project pooling for large sequencing runs.

Services:

• Full or partial Illumina MiSeq runs

- WideSeq for plasmid or other double stranded DNA sequencing
- Quantification of DNA or RNA
- Size and concentration determination
- Library titration
- Consultation for large next generation sequencing projects
- Sample pooling for full lane next generation sequencing

Contact Information: bbcgenomics@purdue.edu

Website: Click here

Research Core/Center: Purdue Imaging Facility/Bindley Bioscience Center Affiliation: Purdue University Director: Andy Schaber, PhD

Description:

The Purdue Imaging Facility enables imaging of all types of biologic and non-biologic samples. Our systems can image samples ranging in size from rodents to extremely small sized objects on glass slides with resolution down to tens of nanometers on our super resolution systems. We train users how to use the imaging instruments and support users in sample preparation, anesthesia, image acquisition and analysis. Our instruments range from high-end confocal and multi-photon microscopes to pre-clinical molecular, μ CT and nuclear imaging systems for both live animal models and non-biologic samples.

Contact Information: Andy Schaber (schaber@purdue.edu) 765-496-3148

Website: Click here

Research Core/Center: Purdue Proteomics Facility Affiliation: Purdue University Director: Uma Aryl, PhD Manager: Jackeline Franco, DVM, PhD

Description:

The Purdue Proteomics Facility (PPF) provides innovative state-of-the-art LCMS/MS analysis of proteins in clinical, environmental and other biological samples. As a shared facility of the Bindley Bioscience Center (BBC) in Discovery Park of Purdue University, the facility enables both targeted and global analysis of proteins, their post-translational modifications and analysis of protein complexes and protein-protein interactions. Coupled with different chromatographic separation techniques, modern mass spectrometric instrumentation, and advanced scientific and bioinformatics expertise, the facility provides unique opportunities for researchers at Purdue and beyond to perform quantitative analysis of proteins in complex biological samples using both global, as well as, targeted proteomic approaches.

- Sample preparation including cell lysis, protein extraction, in-solution and in-gel protein digestion, peptide clean-up
- LC-MS/MS analysis for protein identification, label and label free quantitation, global and targeted proteomics

- Analysis of post-translationally modified proteins and peptides
- MALDI TOF MS analysis of intact protein and peptides
- Gel filtration (SEC) and ion exchange chromatography (IEX) coupled with quantitative MS profiling for the analysis of protein complexes
- Proteomics and phosphoproteomics method development and consultation
- Bioinformatic consultation and support for database searches for protein identification, label and label free quantitation, and data interpretation

Contact Information: Uma Aryl (uaryal@purdue.edu)

Website: Click here

Research Core/Center: Purdue Translational Pharmacology Facility Affiliation: Purdue University Director: Greg Knipp, PhD Manager: Robyn McCain

Description:

The Purdue Translational Pharmacology (PTP) Core conducts in vivo studies that avoid the stressinduced complications of biofluid collection and provide a translational model more closely aligned with drug metabolism in humans. The facility serves individual investigators, government entities and private companies. The PTP synergizes with the Metabolite Profiling Facility in the Bindley Bioscience Center, which facilitates the pharmacological analysis of samples collected during the studies.

Services:

- ADME (absorption, distribution, metabolism, elimination) studies
- Drug formulation studies to test alternate dosage forms
- Pharmacokinetic evaluations of drug candidates
- Bioavailability and first pass metabolism studies (rats)
- Toxicology studies
- Pharmacodynamic studies to examine physiological effects of compounds
- Gross motor activity
- Food and water intake
- Human disease models in swine
- Pre- and post-study support services

Contact Information: Robyn McCain (rrmcain@purdue.edu)

Website: Click here

Research Core/Center: Regenstrief Data Core Affiliation: Indiana University School of Medicine Director: Faye Smith Manager: Katie Allen

Description:

The Regenstrief Data Core is a central point of access to data from the Indiana Network for Patient Care (INPC) and other specialized sources. With a cadre of experienced, full-time data analysts, the Data Core is prepared to help investigators from project start to finish. A data analyst will be in contact with you within two business day of your feasibility or data request. The Data Core has a vision to provide efficient facilitation of research questions from inception to clinical practice. We offer a variety of services, including feasibility and customized data sets, while ensuring compliance with governance and regulations implemented for the safekeeping and handling of protected health information. In addition, Regenstrief Institute manages the Indiana Network for Patient Care (INPC) database on behalf of the Indiana Health Information Exchange (IHIE).

Services:

- Feasibility Assessments
- I2B2
- Cohort Creation
- Recruitment Lists
- Data Linkage
- Natural Language Processing (NLP)
- De-identification
- Registries
- Data Harmonization

Contact Information: Katie Allen (allenkat@regenstrief.org) 317-274-9024

Website: Click here

Research Core/Center: Research Jam

Affiliation: Indiana Clinical and Translational Science Institute, Indiana University School of Medicine **Director:** Sarah Wiehe, MD, MPH **Manager:** Ginal Claxton, MPH, RD

Description:

Research Jam is an interdisciplinary team of healthcare, research, and design professionals. The team uses human-centered design research to collaborate with doctors, patients, and community members in an effort to ensure that health research, interventions, and communications are more relevant to the community they aim to serve. By engaging stakeholders in a co-design process, we are able to assist clients with recruitment strategies, study retention, protocol compliance, dissemination of findings, patient decision-making tools and discovering patient-centered outcomes. Research Jam also includes visual communication and design services that allows us to translate findings and recommendations into figures for grants, posters, brochures, patient interface designs, video story boards, educational material, websites, and more.

Services:

 Research Jam develops and facilitates in-person or virtual sessions using human-centered design to engage stakeholders in exploring a problem space, creating a solution or testing a prototype. Collaborative sessions allow for stakeholders to build-off of the ideas of others and create a sense of community with one another.

- Research Jam creates workbooks that allow stakeholders to provide their perspectives and expertise independently through journaling activities. Workbooks allow stakeholders to engage with us when transportation or topic area create a barrier to participation in a group setting.
- Research Jam creates toolkits that allow stakeholders to provide their perspectives and expertise independently through activities such as submitting videos, audio recordings, photographs, and other hands-on activities. Toolkits allow stakeholders to show aspects of their daily lives and environments.
- Research Jam also helps with cognitive interview development, ethnographic research, and stand-alone activity boards for engaging the public out in the community.
- Design services are offered through Research Jam to provide visual communication assistance when there is not a need for further stakeholder engagement. These range from simple to complex projects with a specialization in figures for grant proposals to quickly communicate complex project ideas or scientific concepts.

Contact Information: pecteam@iupui.edu

Website: Click here

Research Core/Center: Small Animal MRI Facility Affiliation: Purdue University Director: Craig Goergen, PhD Manager: Greg Tamer, PhD

Description:

The Small Animal MRI Facility on Purdue's campus in the Bindley Bioscience Center provides a Bruker 7T small bore MRI system for Purdue users and external users to employ for their MRI needs especially focused on imaging small animals and samples. Personnel are available to assist with experiment planning, implementation, scanning, and analysis.

Services:

• Bruker 7T MRI system with coils, anaesthesia system, and small animal physiologic monitoring system.

Contact Information: Greg Tamer (gtamer@purdue.edu) 765-588-7134

Website: Click here

Research Core/Center: Transgenic and Genome Editing Facility Affiliation: Purdue University Director: Judy Hallett Manager: Judy Hallett

Description:

The TGEF Shared Resource is a state-of-the-art facility that offers a large number of services, including the creation of transgenic, gene knock-in and knock-out mouse and rat models for gain-of-function and loss-of-function experiments. Model systems based on transgenic and knock-in/knock-out strategies provide approaches that are developmentally, anatomically and physiologically relevant to human

disease, and that can supplement traditional xenograft models for testing new anti-cancer therapies. Genome-edited animal models provide valuable reagents for studies ranging from the regulatory mechanisms governing gene expression patterns to cell-cell interactions, cell cycle control and regulation of signal transduction pathways.

Services:

- Mouse/Rat Transgenic Production
- Mouse/Rat CRISPR-mediated Knock Out Production
- Mouse/Rat CRISPR-mediated Knock In Production
- Mouse/Rat Embryo and Sperm Cryopreservation
- Mouse IVF
- Mouse/Rat Strain Rederivation

Contact Information: Judy Hallett (halletje@purdue.edu)

Website: Click here

Research Core/Center: Translation Research Core **Affiliation:** Indiana University School of Medicine **Director:** Kristen Russ, PhD

Description:

The Translational Research Core specializes in assisting researchers with the identification/development and analysis of laboratory correlates in translational research.

Services:

- Protocol Startup
- SOP development
- Sample Retrieval and Management
- Retrieval and logging for storage
- Preparation for analysis
- Blood processing
- Nucleic acid extraction
- Laboratory Analysis
- ELISAs
- Flow Cytometry
- Western Blot
- Protein/nucleic acid quantification
- Comet assays
- Unique assay development

Contact Information: Kristen Russ (karuss@iu.edu) 317-278-4707

Website: Click here

Research Core/Center: UITS Research Technologies Advanced Biomedical IT Core Affiliation: Indiana University Bloomington Director: Robert Henschel Manager: Richard Meraz

Description:

Provide software, technology, and data engineering solutions for research, especially for projects that involve electronic protected health information (ePHI).

Services:

- IU REDCap
- High Performance Storage and Computing
- Custom software development, especially related to REDCap
- Research Technical Project Management

Contact Information: Richard Meraz (rfmeraz@iu.edu) 812-606-5275

Website: Click here