Precision One Health Initiative
UNIVERSITY OF GEORGIA

ONE SCIENCE AT THE INTERSECTION OF PATIENTS, ANIMALS AND OUR ENVIRONMENT

PROGRESS

A Precision One Health Initiative Symposium

Thursday, November 7th, 2024 | 8:30 am - 6:00 pm | UGA Center for Continuing Education

Registration

7:30-8:30 AM

Opening Remarks

8:30 – 9:00 AM *Master's Hall*

Welcome

Dr. S. Jack Hu, Senior Vice President for Academic Affairs and Provost

Symposium Charge

Dr. Jon P. Mochel, Director Precision One Health Initiative

Session 1: Translational Medicine

9:00 - 9:30 AM *Master's Hall*

Dr. Karin Allenspach, Professor of Comparative Medicine

"Using In Vitro and In Vivo Animal Models to Advance Research in Translational Medicine at the University of Georgia"

Moderators: Jon P. Mochel and Brad G. Phillips

Session 2: Systems Modeling and Data Analytics

9:30 - 10:00 AM *Master's Hall*

Dr. Eugene Douglass, Assistant Professor of Pharmaceutical Sciences

"Next Generation Diagnostics: Using "Big Data" to Drive Collaborative Research at the University of Georgia"

Dr. Ritu Pandey, Associate Research Professor, Cellular and Molecular Medicine

"Translational Bioinformatics: Connecting the Bio-Medical Data Points to Enable Precision Medicine"

Moderators: Jon P. Mochel and Brad G. Phillips

Break and Poster Session

10:15 – 11:00 AM *Pecan Tree Galleria*

Graduate Students and Postdoctoral Research Associates

Session 3: Epidemiology and Disease Ecology

11:00– 11:30 PM *Master's Hall*

Dr. Mekala Sundaram, Assistant Professor, Infectious Diseases

"From Knowledge to Action: Integrating Domain Expertise with Predictive Models in Infectious Disease Systems"

Moderators: Jesse Hostetter and Chris King

Session 4: Social Sciences and Medicine

11:30– 12:00 PM *Master's Hall*

Dr. Stephen Correia, Associate Professor of Neuropsychology

"Promoting Cognitive Health in Rural Georgia: Challenges and Progress"

Moderators: Jesse Hostetter and Chris King

Luncheon & Keynote Address

12:15 – 1:45 PM *Magnolia Ballroom Salon*

Introduction

Dr. Sharron Quisenberry, CVM Associate Dean for Research and Faculty And Graduate Affairs

Keynote Speaker

Dr. Yana Zavros, Professor of Cellular and Molecular Medicine, University of Arizona

"Precision Oncology and One Health: a Tale of Two Species"

Breakout Sessions

2:00 – 4:00 PM *Rooms F, G, K, and L*

Room F: Translational Medicine

Panelists: POHI Translational Medicine Core and Affiliate Faculty + Key Stakeholders

Moderators: Karin Allenspach, Anumantha Kanthasamy and Biao He

Room G: Systems Modeling and Data Analytics

Panelists: POHI Systems Modeling Core and Affiliate Faculty + Key Stakeholders

Moderators: : Eugene Douglass, Prashant Doshi and Ping Ma

Coffee Break

3:00 - 3:15 PM

Breakout Sessions (cont.)

Room K: Epidemiology and Disease Ecology

Panelists: POHI Epidemiology Core and Affiliate Faculty + Key Stakeholders

Moderators: Justin Bahl, Sonia Hernandez and Michael Terns

Room L: Social Sciences and Medicine

Panelists: POHI Social Sciences Core and Affiliate Faculty + Key Stakeholders

Moderators: Stephen Correia, Marshall Shepherd and David Olali

Breakout Summary

4:00 – 5:00PM ***Master's Hall***

Next Steps for Advancing the Best Ideas and Immediate Calls for Action

Symposium Conclusion

5:00 – 5:30PM ***Master's Hall***

Concluding Remarks

Dr. Shelley Nuss, Founding Dean, UGA School of Medicine

Closing

Dr. Lisa K. Nolan, Dean, College of Veterinary Medicine

POH Networking Reception

6:00 PM ***Magnolia Ballroom Salon***

Speakers *Biographies & Abstracts*

Dr. Karin Allenspach

Professor of Comparative Medicine

Karin Allenspach Dr. med. vet., FVH, DECVIM-CA, PhD, FHEA, RCVS, AGAF, received her veterinary degree from the University of Zurich. She completed an internship in small animal emergency medicine and critical care at Tufts University, and a residency in small animal internal medicine at the University of Pennsylvania. She is a Diplomate of the European College of Veterinary Internal Medicine and was awarded a PhD in veterinary immunology from the University of Bern, Switzerland for her work on canine chronic enteropathies. Currently, she is employed as a Professor of Comparative Medicine at the University of Georgia, Athens, GA, and is a PI of the SMART Translational Medicine Lab at the University of Georgia, which focuses on developing and culturing adult stem cell-derived organoids from various species. Her latest efforts have resulted in the founding of a start-up company (3D Health Solutions, Inc.) with the goal of commercializing assays for drug screening based on organoid methods.

"Using In Vitro and In Vivo Animal Models to Advance Research in Translational Medicine"

Faculty members of the Translational Medicine (TM) Core of the Precision One Health initiative represent a wide array of specialties, including small and large animal clinicians, pathologists, and infectious disease researchers. The mission of The TM Core is to identify in vitro and in vivo animal models and best practices for advancing precision medicine for both animals and humans. The Core has made significant progress in building competency, resources, and critical mass to accomplish its goals. One of these focus areas is providing access to organoid technology to model both animal and human diseases, as well as access to cutting-edge spatial transcriptomic technologies. In this presentation, we will discuss some recent applications of organoid and spatial transcriptomics technology to inform disease pathogenesis in animals and, translationally, in humans. These studies will serve as examples of how to produce meaningful pilot data to build larger comparative research networks that will attract large federal grant funding.

Dr. Stephen Correia

Associate Professor of Neuropsychology

Stephen Correia, Ph.D., ABPP-CN leads Precision One Health's Social Science and Medicine Core. Dr. Correia is a board-certified clinical neuropsychologist who joined the faculty in the College of Public Health at UGA in August 2022. His academic home is at the Institute of Gerontology and its Cognitive Aging Research and Education (CARE) Center where he serves as the Director of Neuropsychology. Dr. Correia earned his Ph.D. in Clinical Psychology from the University of Rhode Island. His pre-doctoral clinical internship training was at the Malcolm Randall VA Medical Center in Gainesville, Florida, followed by clinical and research post-doctoral fellowships at Brown University where he became a faculty member in Brown's Alpert Medical School. There, he directed neuropsychology internship and fellowship training while serving as the Chief Neuropsychologist at the Providence VA Medical Center from 2005-2019 and then as the Director of Psychology at Butler Hospital in Providence. Dr. Correia's clinical focus is Alzheimer's disease and related dementias, and his research focuses on early detection of dementia, the use of advanced brain white matter imaging methods, and new cognitive test scoring strategies. At the UGA CARE Center, Dr. Correia performs diagnostic evaluations of possible dementia while training UGA's clinical psychology doctoral students. He is active in CARE Center research and community outreach and teaches undergraduate and graduate courses on cognitive aging.

"Promoting Cognitive Health in Rural Georgia: Challenges and Progress"

Cognitive change is a normal part of aging; the significant cognitive and functional decline seen in dementia is not. Alzheimer's disease (AD) is the most common form of dementia, accounting for 60%-80% of all cases. In 2024, it is estimated that 6.9 million individuals aged 65 and older in the U.S. will be living with AD. Georgia has approximately 188,300 cases, which makes up 12% of its population, placing it among the top 10 states with the highest rates in the U.S. While prevalence rates have decreased over the past 25 years, the number of older individuals is expected to continue to grow. The principal investigators from the Social Sciences and Medicine (SSM) Core of the Precision One Health initiative are dedicated to reducing the incidence of AD across Georgia and beyond. Dr. Villa Zapata's work revolves around the economics of medications and the impact of drug interactions that can affect cognition or mimic dementia. Dr. Li's work focuses on the accessibility of new anti-amyloid AD medications, as well as health system preparedness in relation to the availability of specialty diagnostic imaging and monitoring procedures, provider expertise, and infusion centers. Dr. Azevedo's work centers on the use of technology to clearly inform patients of their health status, such as blood pressure, as a means of lowering cognitive risk. Dr. Kiselica, an affiliate of SSM faculty, focuses on utilizing everyday technology (e.g., cell phones) to detect the first cognitive changes in dementia, allowing for early interventions to be implemented. Dr. Correia's work involves educating communities on lowering dementia risk, providing clinical dementia assessments, and collaborating with affiliate faculty member Jennifer Stull on using music to decrease caregiver burden.

Dr. Eugene Douglass

Assistant Professor of Pharmaceutical Sciences

Dr. Douglass has training in physical and organic chemistry, immunology, and computational biology. During his undergraduate work at Worcester Polytechnic Institute, he collaborated with physicists and chemists, publishing first and second author papers on medical diagnostics and photovoltaics, respectively. For his doctoral work at Yale University, he designed, synthesized, and tested small-molecule immunotherapies and fluorescent sensors. He also solved a drug-kinetics problem that had remained unsolved for 70 years. As a postdoctoral researcher, he assisted in building drug-screening and RNA-sequencing infrastructure to support several clinical trials at Columbia University.

"Next Generation Diagnostics: Using "Big Data" to Drive Collaborative Research at the University of Georgia"

The Systems Modeling and Data Analytics (SMDA) Core at the University of Georgia (UGA) is a crucial part of the data-mission of the Precision One Health (POH) initiative. The SMDA Core's mission is to advance collaborative research by utilizing common data types, such as genomics, to bridge communication gaps across traditional academic silos. This mission is pursued through two key objectives: expanding the data workforce by recruiting and training talented individuals and boosting the productivity of current laboratory personnel through enhanced training, collaboration, and automation in data analytics. Two key areas of focus within the SMDA Core are the integration of genomic and drug development datasets, and methodologies across all colleges. These domains are becoming increasingly interconnected as advancements in drug screening technologies allow for precise matching of therapeutic interventions to specific genomic profiles, paving the way for more personalized approaches to medicine. In addition to these priorities, UGA will soon have access to cutting-edge spatial transcriptomic (ST) technologies, which will enable precise measurement of gene expression at single-cell resolution within tissue sections. While ST technologies promise unprecedented insights into in vivo biological processes, they also present significant challenges, particularly in data management and interpretation. These challenges include ensuring data quality, accurate cell typing, and neighborhood analyses, as well as extracting meaningful insights from complex intercellular communication networks. As UGA integrates these technologies, the SMDA Core will play a critical role in addressing these challenges and leveraging the opportunities they present.

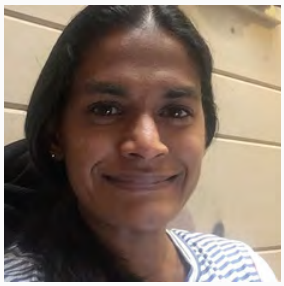
Dr. Ritu Pandey

Associate Research Professor, Cellular and Molecular Medicine

Dr. Pandey is currently the Associate Director of Translational and Clinical Bioinformatics at the Center of Biostatistics and Biomedical Informatics at the University of Arizona Health Sciences. She is also an Associate Research Professor in the Department of Cellular and Molecular Medicine, College of Medicine at the University of Arizona (UA). She received her PhD in Life Sciences from JNU in New Delhi, India. Her postdoctoral work on chromatin remodeling genes at UA contributed to the annotation of the plant genome sequence. As a cancer bioinformatics researcher, she has been working with sequence and genome information, designing and developing bioinformatics applications, analyzing next-generation genome data, and implementing data storage and management programs to integrate genome and clinical data for molecular research. Dr. Pandey has served as an investigator on research grants and as an informatics/bioinformatics core on NIH-funded grants. Over the years, she has mentored several graduate students and served on multiple biological data infrastructure and bioinformatics grant review panels. Her research interests include data-driven discovery of molecular markers and events in pre-clinical models and patient samples using integrated analysis of clinical and molecular data.

"Translational Bioinformatics: Connecting the Bio-Medical Data Points to Enable Precision Medicine"

Translational Bioinformatics (TBI) bridges the gap between genomics and clinical data and emphasizes the use of data-driven methods for storage, processing, analysis, and interpretation of molecular and clinical information. Our goal is to obtain insights into disease biomarkers and therapeutic targets from molecular research while understanding the treatment response and clinical outcome. Vice versa, we aim to gain clinical insights by studying the changes in the molecular landscape of the disease. TBI is central to precision medicine and provides analytics support for datasets from molecular omics, drug screening, imaging, and real-world data from electronic health records. These datasets together comprise the biomedical big data. Our research interest is to investigate molecular events in stratified disease cohorts by integrated computational analysis of clinical and molecular data from multi-omics projects. In this presentation, we will focus on the collaborative infrastructure and resources required for this initiative. We will also present examples of cutting-edge genomics research with patient-stratified populations, which could provide novel indications of therapeutic drugs and targets and inform future clinical trials. This requires multidisciplinary team efforts and has several components that can be uniquely leveraged for the Precision One Health (POH) initiative.



Dr. Mekala Sundaram

Assistant Professor, Infectious Diseases

Dr. Sundaram is a new Assistant Professor appointed by Infectious Diseases and the Savannah River Ecology Laboratory. Her passion for ecology led her to pursue a Master of Science in Conservation Biology at Central Michigan University and later a PhD in Quantitative Ecology from Purdue University's Forestry and Natural Resources program. The ability to utilize quantitative skills is crucial in addressing scientific problems today. Dr. Sundaram has developed a strong background in quantitative work by applying her skills to problems in different disciplines, particularly during her postdoctoral programs at Brown University, Stanford University, the University of Georgia, and Oklahoma State University. She has worked on complex statistical problems at the intersection of ecology, infectious diseases, biochemistry, plant pathology, paleoecology, economics, social sciences, genetics, and geography. She employs techniques such as data mining, maximum likelihood models, Bayesian approaches, text mining, and machine learning to identify animal reservoirs of pathogens, predict disease outbreaks, and understand the transmission of pathogens among hosts. Her current research focuses on disease forecasting and quantifying the potential of zoonotic diseases in species worldwide.

"From Knowledge to Action: Integrating Domain Expertise with Predictive Models in Infectious Disease Systems"

The Epidemiology and Disease Ecology (EDE) Core at the University of Georgia (UGA) utilizes a wide range of approaches to investigate infectious disease outbreaks. Dr. Lokraj Joshi's work is focused on viral evolution, pathogenesis, and the development of new diagnostic and therapeutic technologies using a suite of bioinformatic and molecular tools. Dr. Tatum Mortimer's work centers on epidemiology and the evolution of bacterial pathogens to address global health concerns, specifically antimicrobial resistance. Dr. Douglas Paton utilizes molecular methods such as cloning, tissue culture, biological analysis of multi-omics data, and experimental infections to study how malarial parasites interact with their mosquito vectors. Dr. Daniel Peach's work is focused on arthropod vector ecology, with an emphasis on how vectors interact with their hosts and the environment at large. Dr. Janna Willoughby, an affiliate of the EDE faculty, is focused on the evolutionary genomics of infectious diseases and their animal host populations. Dr. Grazieli Maboni, also an affiliate of the EDE faculty, develops novel diagnostic tools for infectious diseases and is a clinical microbiologist. Dr. Mekala Sundaram's work is focused on forecasting disease outbreak dynamics and developing machine learning applications from mined data. Infectious disease research has made significant strides in understanding the biological mechanisms underlying outbreaks. For many pathogens, there is a wealth of a priori knowledge including data on animal hosts, vaccine targets, evolutionary changes, molecular pathogenesis, socioeconomic triggers, and geographical spread. However, new insights that can help us manage outbreaks can be gleaned by integrating past knowledge from different domains into a comprehensive picture of what drives pathogen spread and emergence. Here, we present three case studies that highlight the power of cross-disciplinary integration and predictive modeling in enhancing our understanding of diverse disease systems. To explore the mechanisms underlying

malaria transmission, we integrate a mosquito agent-based model of expected infection rates, which is parameterized from a priori domain knowledge, with machine learning algorithms to forecast outbreak locations. We explore host jumping for influenza viruses by integrating evolutionary simulations of expected mutational rates with host population dynamics. This enables us to predict cross-species transmission among different mammal populations. We also forecast levels of antimicrobial resistance by incorporating anticipated dose effects from pharmacodynamic models, selection rates from bacterial phylodynamic models, and regional antimicrobial resistance levels defined for specific neighborhoods in a machine learning framework. Our approach, which leverages the integration of domain-specific knowledge with predictive and machine learning techniques, offers new insights into the dynamics of vector borne, bacterial, and evolutionarily adaptable viral pathogens. These insights not only enhance our understanding of pathogen behavior but also inform the development of targeted intervention strategies.

Dr. Yana Zavros

Professor of Cellular and Molecular Medicine
University of Arizona

Dr. Zavros is a gastrointestinal physiologist by training, and her research has largely focused on gastrointestinal disease. While at the University of Cincinnati College of Medicine, she pioneered the use of human gastric and pancreatic organoids to examine underlying mechanisms driving initiation and progression of gastrointestinal cancers, and to serve as invaluable models for therapeutic intervention. While at the University of Arizona, Dr. Zavros served as associated head for research and director of the Tissue Acquisition and Cellular/Molecular Analysis Shared Resource (TACMASR) at the University of Arizona Cancer Center. As the shared resource director, she established the BioDROids(Biology, Development and Research of Organoids) core. As a translational scientist, she leads a multidisciplinary research team comprised of clinicians and scientists with expertise in surgical and medical treatments of pancreatic cancer, pathology and cell biology of the tumor microenvironment, organoid technology, and high-throughput data analysis. This team uses organoid models to investigate the interactions between tumor cells with the tumor microenvironment. By adopting a translational approach using organoids from individual patients suffering from metastatic pancreatic cancer and personalized drug screens to investigate individual responses and to identify combinations of anti-cancer drugs that were most effective for the individual patient. This impactful work has provided insights into cancer cell drug resistance, and it was leveraged to design a Phase II clinical trial that has already made an impact on the lives of patients with pancreatic cancer.Dr. Zavros has extended her studies to Cushing's disease, which is caused by pituitary neuroendocrine tumors. In collaboration with the research team, Dr. Zavros has designed and developed a protocol for the first pituitary neuroendocrine tumor tissue-generated organoid cultures that can be maintained, expanded, and cryopreserved. To leverage this groundbreaking work, a multidisciplinary team of researchers from nine institutions was assembled. The comparison between canine Cushing's, via UGA's veterinary researchers, and human disease is the perfect example of the One Health approach to medicine, which among other things calls for increased collaboration between researchers studying human and animal health. This remarkable team was recently awarded a $14 million NIH RC2 grant to create foundational knowledge of this understudied disease and foster translational research collaborations.

"Precision Oncology and One Health: A Tale of Two Species"

Pituitary neuroendocrine tumors (PitNETs) are rare, understudied tumors that are detrimental to health causing increased mortality and poor quality of life due to either the secretion of excess hormones or from tumor mass effect on critical neurological structures. Cushing's disease (CD) is a rare and serious endocrine disease that is caused by dysregulated adrenocorticotropic hormone (ACTH)-secreting pituitary neuroendocrine tumor (PitNET) that stimulates the adrenal glands to overproduce cortisol. Chronic exposure to excess cortisol causes leads to increased stroke rates, diabetes, obesity, depression, anxiety, and a threefold increase in the risk of death from cardiovascular disease and cancer. The first-line treatment for CD is pituitary surgery, which is followed by disease recurrence in 56% of patients during the 10-year follow-up period. Surgical failures and late recurrences of CD are common, and despite multiple treatments, biochemical control is only achieved in only approximately 50% of patients. Medical therapy is often considered when surgery is contraindicated or fails to achieve remission, or when recurrence occurs. While stereotactic radiosurgery allows therapeutic management of incompletely resected or recurrent PitNETs, its main drawbacks include a longer time to remission (12-60 months) and the risk of hypopituitarism. Despite 40 years of study, therapeutic approaches that overcome therapy resistance and prevent disease and/or tumor recurrence for patients with CD have been incremental. To address this knowledge gap, we have developed human PitNET organoids with a multicellular identity that replicates the patient's own PitNET pathology, function, and complexity. In 2022 the U.S Senate passed a bill forfeiting the need to include noninformative preclinical animal data for the evaluation of therapeutic drug candidates prior to FDA approval. This bill authorizes the use of alternatives to animal testing, including cell-based assays and in silico computational models to assess the safety and efficacy of a candidate drug. As opposed to genetically modified murine models, dogs spontaneously develop PitNETs resulting in forms of CD that closely recapitulate the clinical, histological, immunohistochemical and treatment response features of the human disease. Dogs further exhibit a significantly higher incidence of CD compared to humans (1 in 500 vs. 10 in 1M), which facilitates inclusion of cases to accelerate transition from preclinical research to clinical development of therapeutic drug candidates. Our team's expertise in organoid technology has enabled the first successful development and implementation of this advanced 3D culture in the much-needed PitNET research arena. The development of these advanced in vitro pre-clinical research human and canine organoid research models will provide a resource that will enable the understanding of the complexity PitNET sub-types to develop targeted treatment of PitNETs for "man and potentially man's best friend" to prevent tumor recurrence and ultimately improve patient quality of life. Our proposed studies have the potential to advance our understanding of PitNETs associated with other sub-types of PitNETs including acromegaly and prolactinomas. In addition, Multiple Endocrine Neoplasia type 1, a familial cancer syndrome that will be implemented in the generation of the iPSCs, is classically characterized by the development of neuroendocrine neoplasms in the endocrine pancreas, parathyroid glands, and upper gastrointestinal tract in addition to the pituitary.