January 18, 2022:
Jaline Gerardin, Ph.D.  Assistant Professor, Northwestern University
"Mathematical modeling to inform malaria policy"
Host: Lauren Childs, Ph.D.

January 25, 2022:
Nick W. Ruktanonchai, Ph.D.  Assistant Professor, Department of Population Health Sciences, VA-MD College of Veterinary Medicine
"Using human mobility data to predict and control infectious disease spread" Recorded Video

February 1, 2022:
Andrew Lowell Ph.D., Assistant Professor, Department of Chemistry, and Anne M. Brown Ph.D.  Assistant Professor, Department of Biochemistry
"Overcoming AMR through antibiotic redesign: Coupling computational and experimental science" Recorded Video

February 8, 2022:
Ben Hause, Ph.D.  Assistant Professor, South Dakota State University
"Metagenomic sequencing for virus discovery and characterization" Recorded Video
Host: Kevin Lahmers, Ph.D.

February 15, 2022:
Kim Seed, Ph.D.  Assistant Professor, Department of Plant and Microbial Biology, UC Berkeley
"Fighting with phages: how epidemic Vibrio cholerae defends against viral attack"
Host: Bryan Hsu, Ph.D.

February 22, 2022:
Robyn Klein, Ph.D.  The Robert E. and Louise F. Dunn Distinguished Professor of Medicinal Sciences, Director of the Center for Neuroimmunology and Neuroinfectious Diseases, and Professor of Medicine, Pathology and Immunology, and Neurosciences, Washington University School of Medicine
"Emerging RNA viruses and neurologic sequelae" Recorded Video
Host: Kylene Kehn-Hall, Ph.D.
March 1, 2022:
Jeff Freeman, Ph.D.  Senior Professional Staff in the National Health Mission Area of the Johns Hopkins University Applied Physics Lab
"Evolution of the national COVID-19 response: Lessons learned and a way forward"
Host: Cassidy Rist, Ph.D.

March 15, 2022:
Xinhua Chen, Ph.D.  Assistant Professor of Medicine, Beth Israel Deaconess Medical Center
"C. difficile Infectious --- What Remains Difficult?"
Host: Xin Luo, Ph.D.

March 22, 2022:
James Weger-Lucarelli, Ph.D.  Assistant Professor, Department of Biomedical Sciences and Pathobiology, VA-MD College of Veterinary Medicine
"SARS-CoV-2 Origins and Threat for Spillover Into Animal Reservoirs"  Recorded Video

March 29, 2022:
Townsend Peterson, Ph.D.  University Distinguished Professor, Biodiversity Institute, The University of Kansas
"Distributions of Tick Vector Species in the United States: Shifting Distributional Patterns and Transmission Opportunity" Recorded Video
Host: Luis Escobar, Ph.D.

April 5, 2022:
Eva Harris, Ph.D.  Professor of Infectious Diseases and Vaccinology, UC Berkeley
"The double-edged sword: Dengue and Zika virus pathogenesis and immunity"
Host: Jonathan Auguste, Ph.D.

April 12, 2022:
Rhoel Dinglasan, Ph.D.  Professor of Infectious Diseases and Director of the CDC Southeastern Regional Center of Excellence in Vector Borne Diseases
"Vector-Borne Disease Translational Systems Biology: From discovery to application"

April 19, 2022:
Stacey Schultz-Cherry, Ph.D.  Deputy Director, World Health Organization Collaborating Centre or Studies on the Ecology of Influenza in Animals and Birds,
"Influenza Pathogenesis in Vulnerable Populations"
April 26, 2022:

Oliver Fregoso, Ph.D. Assistant Professor, Microbiology, Immunology and Molecular Genetics, UCLA

"The DNA Damage response in HIV replication and cure"

Host: Nisha Duggal, Ph.D.

May 3, 2022:

Nancy Keller, Ph.D. Professor of Medical Microbiology and Immunology and Bacteriology, University of Wisconsin-Madison

"Co-opting oxylipin signals in fungal disease"

Host: Rana Ashkar, Ph.D.
In the last five years, progress against malaria in the highest-burden countries has stalled or reversed. In response, WHO is leading the High Burden to High Impact (HBHI) initiative. A key pillar of HBHI is the strategic use of data and information to develop national malaria intervention plans that are subnationally tailored to the local context. Our group has been supporting HBHI by developing mathematical models that countries can use to compare the epidemiological impact of candidate intervention plans and to obtain realistic predictions of their plan’s progress toward reaching morbidity and mortality reduction targets. I present our modeling approach for Nigeria in the context of Nigeria’s implementation of HBHI in partnership with WHO.
New technologies such as GPS trackers and mobile phones have not just revolutionized how people stay connected and navigate the world, but also have provided unparalleled insight into how communities move, potentially spreading infectious diseases as they travel. Using human mobility data from mobile phones and smartphones, we have been able to identify key high-risk populations for diseases such as malaria based on their travel patterns, and predict where emerging diseases such as COVID-19 will spread next, towards improving intervention strategies. Here we present some recent advances in epidemiology enabled by mobility data, and discuss how these data could be used in the future to improve epidemic control.
There is an urgent call to identify new drugs, improve on usage specificity, and iterate on previous drug scaffolds to improve efficacy. Recent structural advancements and enhanced computational biochemistry methodologies enables us to refine mechanistic insight into antibiotic/cellular-target interactions at an atomistic level and to accurately tailor drug functional group activity. Our interdisciplinary collaboration between computational biochemistry and synthetic chemistry is developing new fields of antibacterial research, enabling both the improvement of existing antibiotics and the hybridization of two active drugs into novel bidentate antibiotics that engage two cellular targets simultaneously. These approaches work to overcome the increasing societal burden of antimicrobial resistance.
Metagenomic sequencing is increasingly being utilized for veterinary diagnostic testing. The strengths of metagenomic sequencing include the ability to detect microorganisms without a prior knowledge of their sequence and the ability to detect numerous microorganisms concurrently. Cases with unusual clinical presentations, cases where expected pathogens are not detected, and “complex” diseases present ideal situations for metagenomic sequencing and have led to the discovery of numerous significant viruses. Application of metagenomic sequencing to diagnostic samples collected at the domestic and wildlife interface is increasingly being used to identify potential emerging viruses that threaten human and livestock health. For example, sequencing of bats submitted to our laboratory for rabies virus testing has recently identified numerous novel viruses, including members of Retroviridae, Paramyxoviridae, Rhabdoviridae, Picornaviridae, and Coronaviridae.
The arms race between genomic parasites like viruses and their cellular hosts is a key force shaping the evolution of all forms of life. Bacterial viruses (phages) profoundly impact the evolution of their bacterial hosts, both through predation, which selects for hosts with defenses that overcome phage killing and through mobilization and dissemination of genetic material. Certain mobile elements, the phage satellites, have evolved sophisticated mechanisms to exploit phages for their own selfish spread. Such elements interfere with the replication of the phages they parasitize, and as such, provide their cellular hosts with a means to reduce phage predation. Our lab discovered PLEs (for phage-inducible chromosomal island-like elements) in Vibrio cholerae that provide a specific and robust defense against the dominant lytic phage co-circulating with epidemic V. cholerae strains. Our efforts to understand the molecular mechanisms underpinning PLE activity and phage-encoded mechanisms to counter PLE activity will be discussed.
Our distinguished speaker, Dr. Robyn Klein will be here in person presenting this week. We hope you will join us at Fralin Hall Auditorium

"Emerging RNA viruses and neurologic sequelae"

One of the most debilitating consequences of certain viral infections, including those that do not invade the central nervous system, is impairment in memory and learning that occurs in over 50% of survivors, despite recovery from acute infection. I will discuss some of the research conducted in my lab at Washington University School of Medicine focused on mechanisms of cognitive impairment due to arboviral infections that may also occur in cases of COVID-19.

Zoom Link: https://virginiatech.zoom.us/j/89419666443
Center for Emerging, Zoonotic, and Arthropod-borne Pathogens (CeZAP) Distinguished Speaker Seminar Series in Infectious Diseases

Tuesday, March 1, 2022 at 12:30 pm
Zoom Link: https://virginiatech.zoom.us/j/89419666443

SARS-CoV-2, the worst pandemic in over 100 years, has severely strained our Nation’s health system and presented critical challenges to public health agencies at all levels of government.

In March 2020, in the early stages of the response, the Johns Hopkins Applied Physics Laboratory (APL) was asked to mobilize a large team in support of the White House COVID-19 Task Force. APL remains a key player in the response today. Lessons learned from the APL team throughout the response will be presented along with a vision for enabling a more effective response to future health threats.
**C. DIFFICILE INFECTION ---WHAT REMAINS DIFFICULT?**

**MARCH 15, 2022 AT 12:30 PM VIA ZOOM**

**Xinhua Chen, Ph.D.**

Assistant Professor in Medicine
Harvard Medical School
BETH ISRAEL DEACONESS MEDICAL CENTER

**Center for Emerging, Zoonotic, and Arthropod-borne Pathogens (CeZAP)**

**Distinguished Speaker Seminar Series in Infectious Diseases**

**Tuesday, March 15, 2022 at 12:30 pm**

**Zoom Link: https://virginiatech.zoom.us/j/89419666443**

*Clostridioides difficile* is a leading nosocomial pathogen and a growing community-acquired infection worldwide. Despite advances in the understanding and diagnosis of *Clostridioides difficile* Infection (CDI), it remains difficult for clinicians who care for patients with CDI to distinguish active infection from *C. difficile* carriage. Currently none of the available clinical tests for *C. difficile* can adequately make this distinction. The pendulum has swung from a focus on rapid molecular diagnosis such as PCR to a call for use of algorithmic approaches. In this presentation, we present multiple published and unpublished approaches to help address this challenge. We will also present recently discovered mechanism of action of *C difficile* toxins, which may also shed light on understanding of host immune responses in distinguishing active infections from asymptomatic carriage of this difficult bug.
SARS-CoV-2 likely emerged into humans from bats, possibly through an intermediate host species. The viral mutations that mediated this jump from animal reservoirs are poorly understood. Furthermore, as SARS-CoV-2 has explosively spread through humans, several reverse zoonosis events have occurred where animals like mink, hamsters, and deer have been infected and transmission within these species has occurred. Perhaps more alarmingly, the virus was transmitted back into humans from these animal species. I will discuss our ongoing experiments seeking to understand how SARS-CoV-2 emerged into humans from animal reservoirs, and how its spillover into new animal reservoirs might impact future waves of infection.
Geographic distributions of species are a function of multiple factors (Grinnellian ecological niche, biotic interactions, dispersal potential), such that range expansions reflect responses to complex phenomena. In this talk, I will contemplate range shifts in ticks and the pathogens that they carry, in the context of examples of range stasis (forest-restricted herps in the eastern Great Plains) and range expansion (Snail Kites in Florida), assessing the questions of (1) whether the tick range expansions are real, (2) what are the drivers of tick range expansion, and (3) the status of pathogens in range-edge and/or expanding populations. The picture is decidedly complicated, such that range dynamics are complicated to predict, and their study must be multi-dimensional in nature.
The four dengue virus serotypes (DENV1-4) and the related Zika flavivirus (ZIKV) are responsible for the most prevalent mosquito-borne viral diseases of humans. This lecture focuses on two aspects: pathogenesis and protection mediated by the flavivirus nonstructural protein 1 (NS1) and the protective as well as disease-enhancing role of the flavivirus antibody response. We have described a novel role for NS1 in triggering hyperpermeability of human endothelial cells and systemic vascular leak in vivo via disruption of the endothelial glycocalyx layer and intercellular junctions. We have made progress elucidating the mechanisms and molecular determinants of these pathogenic processes and have shown that flavivirus NS1 proteins modulate endothelial barrier function in a tissue-specific manner in vitro and in vivo, reflecting the pathophysiology of each flavivirus. We have also demonstrated the potential of NS1 as a vaccine component and defined the mechanism of protective anti-NS1 antibodies using in vitro and in vivo model systems. Studying the immune response to DENV and ZIKV in our long-standing cohort study in Nicaragua, we have shown that different antibody titers and Fc effector functions can either protect against symptomatic DENV infection or enhance dengue disease severity. Interestingly, we found that prior DENV infection and cross-reactive antibody titers are protective against subsequent ZIKV disease in the cohort study, whereas prior ZIKV infection enhances subsequent DENV2 disease, with implications for vaccine development. Overall, this multidisciplinary approach reveals the complexity of flavivirus pathogenesis and immunity using in vitro and animal models as well as studies in human populations, and sets the stage for identifying new drug targets and vaccine components for flaviviral diseases.

Center for Emerging, Zoonotic, and Arthropod-borne Pathogens (CeZAP)
Distinguished Speaker Seminar Series in Infectious Diseases

Tuesday, April 5, 2022 at 12:30 pm
Dr. Eva Harris will be here in person presenting this week.
Join us at Fralin Hall Auditorium

The four dengue virus serotypes (DENV1-4) and the related Zika flavivirus (ZIKV) are responsible for the most prevalent mosquito-borne viral diseases of humans. This lecture focuses on two aspects: pathogenesis and protection mediated by the flavivirus nonstructural protein 1 (NS1) and the protective as well as disease-enhancing role of the flavivirus antibody response. We have described a novel role for NS1 in triggering hyperpermeability of human endothelial cells and systemic vascular leak in vivo via disruption of the endothelial glycocalyx layer and intercellular junctions. We have made progress elucidating the mechanisms and molecular determinants of these pathogenic processes and have shown that flavivirus NS1 proteins modulate endothelial barrier function in a tissue-specific manner in vitro and in vivo, reflecting the pathophysiology of each flavivirus. We have also demonstrated the potential of NS1 as a vaccine component and defined the mechanism of protective anti-NS1 antibodies using in vitro and in vivo model systems. Studying the immune response to DENV and ZIKV in our long-standing cohort study in Nicaragua, we have shown that different antibody titers and Fc effector functions can either protect against symptomatic DENV infection or enhance dengue disease severity. Interestingly, we found that prior DENV infection and cross-reactive antibody titers are protective against subsequent ZIKV disease in the cohort study, whereas prior ZIKV infection enhances subsequent DENV2 disease, with implications for vaccine development. Overall, this multidisciplinary approach reveals the complexity of flavivirus pathogenesis and immunity using in vitro and animal models as well as studies in human populations, and sets the stage for identifying new drug targets and vaccine components for flaviviral diseases.
The objective of Translational Systems Biology (TSB) is to understand the bigger biological picture by weaving together genomic, transcriptomic, proteomic and metabolomic features of a biological system that are profiled under a given condition (e.g., infection, drug treatment, insecticide exposure). This is an iterative process wherein seminal hypotheses result in the generation of new data that can inform development of new analytical tools, which in turn generate new data and hypotheses, and so forth. Within each successive round of hypothesis-interrogation-insight, TSB opens avenues to transition molecular insights into public health interventions. The goal of the talk will be to provide examples of TSB in action in the context of vector-borne disease research.
A high body mass index (BMI) is associated with more severe influenza infection, prolonged viral shed, and poor vaccine efficacy. In this talk, we will explore how a high BMI or poor metabolic syndrome influences epithelial immunity through the upregulation of a specific integrin, and the subsequent impact on infection and vaccination. Finally, we will discuss weight loss as a means to modulate these responses.
The DNA damage response in HIV replication and cure

The overall goal of our work is to better understand virus-host interactions that regulate lentiviruses such as HIV-1. We take a unique interdisciplinary approach to study these interactions by combining molecular virology, biochemistry, and evolutionary biology. We have identified the host DNA damage response (DDR) proteins and pathways as important regulators of lentiviral replication. We are currently working to understand the roles of the DDR in lentiviral replication and to determine if these pathways can be modulated to help cure HIV. Through our studies we hope to uncover novel aspects of lentiviral biology that can lead to enhanced measures in controlling HIV.
Co-opting oxylipin signals in fungal disease

Oxylipins, or oxygenated lipids, are universal signaling molecules across all kingdoms of life. In the filamentous fungal pathogen Aspergillus fumigatus, oxylipins – both fungal and host derived – mediate developmental switches in development such as hyphal branching and spore production.

In vertebrate hosts, oxylipins activate either pro- and anti-inflammatory pathways that can exacerbate or resolve microbial disease. The secreted A. fumigatus oxylipin 5,8-diHODE induces hyperbranching via activation of the fungal transcription factor ZfpA (1). Here we explore virulence attributes of ZfpA deletion and overexpression mutants in the zebrafish model of invasive aspergillosis and address the hypothesis that the vertebrate oxylipin receptor G2A may recognize 5,8-diHODE and play a role in host response to A. fumigatus infections.