

**CREID Network
2021 Pilot Program Awardees**

Principal Investigator	Issa Abu-Dayyeh, PhD Science and Research Supervisor, Research and Development Department, Biolab Diagnostic Laboratories
Title	Development of a Real-Time Pathogen Surveillance System in Jordan
Pathogen Focus	SARS-CoV-2
Country	Jordan, US
Collaborating CREID Research Center	WARN-ID
Abstract	<p>The proposed collaboration between Biolab and WARN-ID aims to develop a public health pathogen genomic surveillance and outbreak response system to help inform public health interventions during the current SARS-CoV-2 pandemic and in future epidemics. Biolab has publicly released 584 SARS-CoV-2 genomes. The majority were resequenced and curated by our collaborators in the Andersen Lab at The Scripps Research Institute. Only select samples were sequenced in-house by Biolab owing to financial resource constraints and a lack of experience with the required bioinformatic pipelines, limiting our ability to undertake the large-scale next-generation sequencing required for sustainable in-country pathogen surveillance. This project aims to investigate the circulating and emerging diversity of SARS-CoV-2 in Jordan. The secondary aim is to establish a training platform to develop in-country next generation sequencing (NGS) capacity, equipping local scientists with the necessary bioinformatic skillset to process, analyze, and share pathogen sequence data. We will use a hypothesis-driven sampling framework to enrich our dataset with the viral genomes most likely to harbor genetic changes of epidemiological or clinical interest to maximize the informativeness of our proposed sample size of 500 genomes. The sampling framework will include (1) patients with recurring SARS-CoV-2 infections, (2) patients infected with SARS-CoV-2 despite Spike antibody seropositivity, and (3) infected traveling foreigners and expats. The data generated will provide WARN-ID labs and the global genomic epidemiology community with valuable information to fill the gaps on the global circulating diversity of SARS-CoV-2, adding critical value to understanding the epidemiology of SARS-CoV-2 in Jordan and the Middle East.</p>

Principal Investigator	Daniel Moura de Aguiar, PhD Professor, Faculty of Veterinary Medicine, Federal University of Mato Grosso
Title	Revealing Vector Species with Potential to Mediate Pathogen Spillover from Wildlife to Livestock in the Pantanal
Pathogen Focus	Arboviruses
Country	Brazil
Collaborating CREID Research Center	CREATE-NEO
Abstract	<p>Pathogen emergence is generally initiated by spillover of a pathogen from wildlife into livestock or humans, which can occur in areas with high animal and arthropod biodiversity that act as bridge vectors, such as ticks. The Pantanal in Brazil is a critical scenario for this occurrence, as is the largest wetland in the world and a global biodiversity hotspot. The periodic flooding that characterizes the Pantanal habitat prevents major ecosystem modification, cattle and horses are ranched extensively at relatively low densities, enabling preservation and intermixing with the diverse wildlife and their ticks. We hypothesize that potential tick vectors co-occur with both wildlife and livestock within the Pantanal and thereby have the potential to affect spillover. To test this hypothesis, we will monitor the occurrence of wildlife, livestock, and ticks at replicate sites in the Pantanal across the project using a combination of camera traps, collection, and tick identification. The outputs of this analysis will be used to guide the targeted screening of a subset of individual ticks for particular arboviruses using next-generation sequencing. Climates and geographical location data will be analyzed in conjunction with remotely sensed abiotic variables to characterize environmental predictors of transmission risk posed by ticks to domestic species in this region. Machine learning on traits of collected ticks will be used to discern vector species and individual ticks and hosts that are most likely to be involved in the wildlife cycle of target pathogens, particularly arboviruses. The study benefits CREATE-NEO by expanding capacity for investigation of tick-borne viruses.</p>

Principal Investigator	Nguyen Van Cuong, DVM, PhD Centre for Tropical Medicine, Oxford University Clinical Research Unit
Title	Mixed-species farming, viral diversity, and risks of cross-species transmission in the Central Highlands of Viet Nam
Pathogen Focus	Zoonoses, Coronaviruses, Paramyxoviruses
Country	Viet Nam
Collaborating CREID Research Center	EID-SEARCH
Abstract	<p>Viet Nam sits within a critical Southeast Asian emerging infectious disease hotspot with diverse wildlife and a rapidly increasing human population. In this region, wildlife farming is a growing but inadequately regulated industry that exhibits many features thought to contribute to increased risks of cross-species transmission and zoonotic disease emergence. We will focus on a key zoonotic disease pathway that was involved in the emergence of Nipah virus, SARS-CoV, and potentially SARS-CoV-2—the spillover of viruses from wildlife to multispecies farms, and subsequently to people. We will test a key hypothesis: viral diversity and cross-species transmission will increase with species diversity on mixed-species farms, and this pattern will be further amplified by the presence of wildlife species. We will access a previously untouched sample set from 64 mixed-species farms in a biodiverse region of central Viet Nam where wildlife and domestic species are farmed both together and separately. We will characterize viral diversity in single- and mixed-species farms using metagenomics and PCR, identify their zoonotic potential using ecological and phylogenetic methods, and estimate risk of emergence by analyzing distribution and prevalence. To inform the local community of our results, we will develop a two-way dialog with farmers and government stakeholders in Viet Nam regarding potential disease risks associated with wildlife and mixed-species farming. Importantly, this project builds capacity for emerging infectious disease research in Southeast Asia by supporting the in-country development of analytically robust, hypothesis-driven research into the ecology and evolution of emerging infectious diseases.</p>

Principal Investigator	Betania Drumond, PhD, MSC Assistant Professor, Microbiology, Federal University of Minas Gerais
Title	Investigation of the spatiotemporal dynamics and ecological drivers of enzootic arboviruses circulation in non-human primates in Minas Gerais state/Southeast Brazil
Pathogen Focus	Yellow fever virus and Mayaro virus
Country	Brazil
Collaborating CREID Research Center	CREATE-NEO
Abstract	<p>Recent outbreaks of yellow fever virus (YFV) have spread from the Amazon Basin into heavily populated southeastern Brazil. Despite this incursion into urbanized areas, to date, all human infections appear to result from spillover from infected non-human primates (NHPs). We hypothesize that recent yellow fever outbreaks reveal a previously unappreciated level of connection, via mosquitoes, between humans and NHPs in eastern Brazil, which may lead to a spillover of additional arboviruses. Our objectives are to characterize the spatiotemporal dynamics and ecological drivers of YFV circulation in NHPs and investigate whether Mayaro virus (MAYV) also broke out in NHPs concurrently with the YFV outbreak. We will quantify active infection or previous exposure of free-living NHPs to YFV or MAYV by RT-PCR and neutralizing antibody assays, respectively. Then we will identify the biotic and abiotic drivers of viral infection using spatiotemporal statistical models, with local environmental factors and new host-level traits as explanatory variables. Our goals are to predict the possible hosts and geographic extent of YFV and MAYV transmission and dynamics. These findings will guide future efforts on viral surveillance. Health authorities could use our inferences to strengthen vaccination programs and prioritize surveillance and control strategies. The results could also be translated into modeling efforts on other enzootic viruses supporting public health decisions to prevent and cope with future outbreaks. The project will expand the PI's research capacity for detecting viruses and identifying ecological drivers of viral transmission.</p>

Co-Principal Investigator	Bronwyn Gunn, PhD Assistant Professor, Paul G. Allen School of Global Health, Washington State University
Co-Principal Investigator	Robert Langat, PhD Senior Scientist, Kenya AIDS Vaccine Initiative—Institute of Clinical Research (KAVI-ICR), University of Nairobi
Title	Defining antiviral humoral immunity against SARS-CoV-2 in Kenya
Pathogen Focus	SARS-CoV-2
Country	Kenya
Collaborating CREID Research Center	CREID-ECA
Abstract	<p>The SARS-CoV-2 pandemic has resulted in >115 million infections with >2.5 million deaths worldwide, yet Kenya has reported <110,000 infections and <2,000 deaths. A recent serosurvey conducted by the Centers for Research in Emerging Infectious Diseases East and Central Africa (CREID-ECA) in Nairobi indicates that approximately 35% of the population in the capital city (>1 million people) had been infected/exposed to SARS-CoV-2 by November 2020 yet this has not been accompanied by overwhelming reports of hospitalization or death. Protective humoral immunity that limits infection, dissemination, and transmission is thought to be critical in preventing development of severe disease; thus, individuals within Kenya may have unique humoral profiles that provide protection against severe disease. However, the recent emergence of SARS-CoV-2 variants with increased transmission and immune evasion properties have threatened to undermine preexisting humoral immunity established prior to November 2020. Thus, in this Pilot Program, we propose to characterize antiviral humoral immunity that developed in Kenya throughout the SARS-CoV-2 pandemic (March-November 2020) and determine if immunity is compromised in the context of emerging global and Kenyan/East Africa regional SARS-CoV-2 variants. We will analyze existing sera samples collected by CREID-ECA and the University of Nairobi for Fab-mediated neutralization and Fc-mediated innate immune effector functions using established Systems Serology and pseudo neutralization platforms. The proposed objectives will inform on the magnitude and quality of humoral immunity in the Kenyan population and determine if emerging variants are resistant to preexisting antibodies generated early in the pandemic to help guide public health policy and vaccine strategies.</p>

Principal Investigator	Janin Nouhin, PhD Scientist, Virology Unit, Pasteur Institute of Cambodia
Title	Hantavirus Detection and Characterization in Rodents and Human Seroprevalence Study in Cambodia
Pathogen Focus	Hantavirus
Country	Cambodia
Collaborating CREID Research Center	PICREID
Abstract	<p>Hantaviruses are widespread across the world and remain a threat to public health. They are maintained in the environment via persistent infection in reservoirs such as rodents and transmitted to humans through inhalation of aerosols containing animal excreta. Data of hantavirus from South-East Asia remain scarce. In Cambodia, the presence of hantavirus in rodents was reported for the first time in 1998. In humans, data are still lacking and the burden of the disease remains unknown. The purposes of the study are (1) to develop and standardize serological and molecular tools for diagnosis and characterization of hantavirus; (2) to document the presence and diversity of hantaviruses among rodents in urban and rural areas of Cambodia; and (3) to study the prevalence of hantavirus infection in humans and identify factors associated with hantavirus infection or exposure. This is a retrospective study nested in the HEPAR project in which rodent and human samples have been collected from urban and rural areas of Cambodia. The study will be conducted in collaboration with various units of Institut Pasteur Paris, which is part of the Pasteur International Center for Research on Emerging Infectious Diseases. The proposed study will provide a wide range of diagnostic tools, a better understanding of hantavirus circulation in Cambodia, and help us expand our other fundamental research questions including study of hantavirus pathogenesis using in vitro experiments, study of viral persistence in the environment, and search of evidence of acute hantavirus infection in patients.</p>