2023 CREID Pilot Program Awardees

Principal Investigators	**Ngu Njeu Abanda, PhD, Centre Pasteur du Cameroon**
Title	***Reconstructing historical patterns of arbovirus transmission in Cameroon using serological data***
Pathogen Focus	Arboviruses
Country	Cameroon
Collaborating CREID Research Centers	WAC-EID, PICREID
Abstract	Arboviruses such as chikungunya, dengue, o'nyong-nyong, and Zika have re-emerged over the last decades causing epidemics, illness, and death. Surveillance of these arboviruses is critical to help track transmission and guide public health interventions. Unfortunately, most at-risk countries lack appropriate arbovirus surveillance systems. As such, the long-term epidemiology, population immunity, and annual infection risk of these arboviruses are grossly underestimated and poorly understood. Spatially explicit age-stratified serological surveys can provide a cost-efficient way of estimating the magnitude of arbovirus infections and understanding past infection risk in different locations. Generally, individuals exposed to arboviruses develop specific long-lived antibodies. Since age usually reflects the duration of exposure, age-stratified serological surveys carried out at one-timepoint or over repeated intervals, allow accurate assessment of arbovirus incidence over time and space in a population. For this Pilot Program study, Dr. Abanda will use an existing sample set of over 20,000 plasma/serum samples from all health districts in Cameroon, collected each year from 2010 to 2022, to determine population exposure to arboviruses. To maximize the insights we can gain from these samples, we will fit age-stratified serological data to mathematical models to estimate the annual incidence and reconstruct the historic transmission patterns of these arboviruses over a 60-year period. This study will provide a detailed understanding of where outbreaks of arboviruses are likely to occur and the spatial reach of previous outbreaks. Through the proposed study, the Dr. Abanda will receive specialized training on immunological techniques, and mathematical modeling, and be guided in the process by experienced mentors. Dr. Abanda is a Research Scientist in the Department of Virology with the Centre Pasteur du Cameroon. He will be mentored by Dr. Scott Weaver, PI of WAC-EID, and Chair of the Department of Microbiology and Immunology at University of Texas Medical Branch, Dr. Henrik Salje, lecturer in the Department of Genetics at the University of Cambridge, and Dr. Richard Njouom, head of the Department of Virology at the Centre Pasteur de Cameroon

Principal Investigator	**Christian Ranaivoson, PhD** **Association Ekipa Fanihy**
Title	***Development of a comprehensive serological, molecular, and genomic surveillance platform for potentially zoonotic bat-borne viruses in Madagascar***
Pathogen Focus	Henipaviruses
Country	Madagascar
Collaborating CREID Research Center	CREID-ESP
Abstract	Bats are natural reservoirs for the world's most virulent viral zoonoses, including Hendra and Nipah henipaviruses, Ebola and Marburg filoviruses, and SARS, MERS, and SARS-CoV-2 coronaviruses. Fruit bats known to host potentially zoonotic henipaviruses, coronaviruses, and filoviruses are consumed widely as a source of human food in Madagascar, offering substantial opportunity for zoonotic transmission. In 2022, the Association Ekipa Fanihy, a nonprofit focused on disease ecology and bat conservation in Madagascar, identified a novel henipavirus, Angavokely virus (AngV), in urine collected from wild Madagascar fruit bats. The viral genome of AngV suggests that it has significant pathogenic potential, were it to spillover to humans, highlighting the importance of heightened surveillance for henipavirus-associated zoonotic risk in Madagascar. In this CREID Pilot Program, Dr. Ranaivoson plans to establish a platform for serological, molecular, and genomic surveillance of bat-borne henipaviruses on the campus of Madagascar Biodiversity Center in Antananarivo, Madagascar. Ultimately, Dr. Ranaivoson aims to establish a longitudinal time series of wild fruit bat serological and infection status data that will inform both statistical and mechanistic models forecasting henipavirus shedding into the surrounding environment—and corresponding zoonotic risk. Only through wild bat surveillance and serological and molecular sample assay in Madagascar will this work be achieved on a timeline that is adequate to inform public health action to prevent future zoonoses. Dr. Ranaivoson is the Director of the Association Ekipa Fanihy and will be mentored by Dr. David Wang, PI of CREID-ESP and Professor of microbiology and pathology and immunology at the Washington University School of Medicine in St. Louis and Dr. Cara Brook, Assistant Professor in the Department of Ecology and Evolution at the University of Chicago.

Principal Investigators	**Miguel Garcia Knight, PhD** **National Autonomous University of Mexico**
Title	***Virome diversity across ecological niches in mosquito vectors***
Pathogen Focus	Arboviruses
Country	Mexico, Uganda
Collaborating CREID Research Centers	EpiCenter, WAC-EID
Abstract	The viromes of mosquitos that transmit arboviruses mainly consist of insect-specific viruses (ISVs). Mounting evidence suggests that ISVs can 1) modulate arbovirus transmission and 2) form a stable core virome in some mosquito species. However, the factors that modulate virome composition are poorly understood. For this Pilot Program study, Dr. Garcia Knight will focus on virome diversity in *Ae. aegypti formosus* (Aaf) and *Ae. aegypti aegypti* (Aaa) subspecies that have contrasting susceptibilities to arboviruses. Dr. Garcia Knight hypothesizes that core ISVs differ in Aaa and Aaf viromes and that ISV diversity is lower in Aaf. The study will also focus on correlates of virome diversity of additional mosquito species sampled over a gradient of environmental degradation. Dr. Garcia Knight will assess if core viromes are a common feature in mosquito species and the taxonomic rank at which they are structured. Finally, he will compare the antiviral immune responses to core and non-core ISVs and to arboviruses across mosquito species. To address these aims, Dr. Garcia Knight will compare mosquito populations from Western Uganda and the Yucatan peninsula in Mexico, two regions with a rich history of arbovirus research. The study will use complementary deep sequencing approaches and robust computational metagenomic analysis methods to determine virome composition in 150 pools of *Aedes* and *Culex* mosquitoes collected by parent studies. Study results will help assess whether ISVs play a role in arbovirus outbreak dynamics and whether virome composition and diversity is influenced by environmental factors such as habitat degradation. Ultimately, study results will help seed future studies focused on novel intervention strategies to limit arbovirus epidemics. Dr. Garcia Knight is with Instituto de Investigations Biomedicas in the National Autonomous University of Mexico and will be mentored by Dr. Lark Coffey, Associate Professor in the Department of Pathology, Microbiology, and Immunology in the School of Veterinary Medicine at the University of California Davis, and Dr. Andrew Routh, Associate Professor in the Department of Biochemistry and Molecular Biology at the University of Texas Medical Branch.

Principal Investigators	**Francesca Falconi Agapito, PhD, Universidad Peruana Cayetano Heredia** **Phillippe Selhorst, PhD, Institute of Tropical Medicine Antwerp**
Title	***Application of mNGS to identify etiologies of acute undifferentiated fever in the Peruvian Amazon***
Pathogen Focus	Viruses causing acute undifferentiated febrile illnesses
Country	Peru
Collaborating CREID Research Center	EpiCenter
Abstract	In the tropics, approximately 50% of patients with acute undifferentiated febrile illnesses (AUFI) remain undiagnosed. Differential diagnosis, important to guide treatment and case management, is challenged by several factors including a broad variety of (un)known pathogens causing AUFI, large range of overlapping symptoms making clinical diagnoses unreliable, epidemiological synergy between shared vectors and geographic distribution of etiologies, and limited laboratory capacity. To date, approaches used for the identification of AUFI etiologies mostly rely on targeted tests for few pathogens, while pathogen coinfections remain understudied because once a pathogen is detected, others are rarely sought. Drs. Falconi Agapito and Selhorst's study objective is to implement metagenomic sequencing on Oxford Nanopore's minION platform and evaluate the potential impact of this technology on standard clinical diagnostics and care, pathogen surveillance, and public health. Using retrospective serum samples collected from AUFI patients between 2018-2021 in Yurimaguas and Iquitos, this study aims to (1) evaluate the utility of nanopore metagenomics in absence of a diagnosis employing samples that tested negative to Dengue virus, Zika virus, yellow fever virus, Chikungunya virus, malaria and Leptospirosis; (2) evaluate the added value of nanopore metagenomics for samples with an existing diagnosis on samples positive to Dengue virus; and (3) evaluate the cost-effectiveness of metagenomic nanopore diagnostics and surveillance in Peru. This CREID Pilot study will develop the necessary knowledge and infrastructure to perform metagenomic sequencing and to conduct follow up studies using full genome sequences of those pathogens to answer specific epidemiological questions (spread, origin, source) and the possible implication of viral evolution in disease severity, resistance, and transmissibility. Dr. Falconi Agapito is a postdoctoral fellow in the Virology Unit at the Universidad Peruana Cayetano Heredia and Dr. Selhorst is a researcher in Biomedical Sciences at the Institute of Tropical Medicine Antwerp. They will be mentored by Dr. Amy Morrison, Project Scientist in Pathology, Microbiology, and Immunology in Veterinary Medicine at the University of California Davis.

Principal Investigators	**Bianca Bratuleanu, PhD, Iasi University of Life Sciences** **Sarah Temmam, PhD, Institut Pasteur**
Title	***Arbovirus discovery and surveillance in Danube Delta Biosphere Reserve, Romania***
Pathogen Focus	Arborviruses
Country	Romania, France
Collaborating CREID Research Center	PICREID
Abstract	Ticks are hematophagous arthropods responsible for major human and animal diseases. They carry microbial communities that include symbionts, commensals, and pathogens. The geographical distribution of ticks is expanding worldwide, leading to the appearance of risks of emergence of tick-borne diseases in naïve areas. Tick dispersal over long distances occurs concomitantly to vertebrate animal movement, for example migratory birds. In Eastern Europe, the Danube Delta constitutes an important wetland area for birds that migrate between Europe and Africa, favoring the emergence of pathogens through animal/arthropod exchanges. In this Pilot Program study, Drs. Bratuleanu and Temmam will investigate the interrelationships between tick, avian, rodent, and livestock viruses in the Danube Delta biosphere. With the identification of novel tick-borne arboviruses and their vertebrate hosts, the co-PIs want to decipher the ecological cycle of tick-borne viruses at the vector and vertebrate reservoir levels to evaluate the risk of importation of tick-borne arboviruses to new areas via migratory birds. The knowledge generated in this study will be key for improving targeted surveillance of tick-borne arboviruses. Using state-of-the-art high-throughput sequencing and bioinformatics techniques, Drs. Bratuleanu and Temmam will characterize the virome of different life stages of ticks. They will search for infection by candidate arboviruses in wild and domestic animals exposed to ticks using targeted serological tests. Dr. Bratuleanu will conduct entomological surveys and the characterization of tick viral communities using deep sequencing and phylogenetic studies, with the support of Dr. Temmam. Dr. Temmam will be responsible for the determination of vertebrate host spectrum of candidate tick-borne arboviruses. Dr. Brauleanu is with the Regional Center of Advanced Research for Emerging Diseases, Zoonoses and Food Safety at Iasi University of Life Sciences and Dr. Temmam is with the Pathogen Discovery Lab at Institut Pasteur. They will be mentored by Sarah Bonnet, Institut Pasteur and Marc Eloit, Professor of Virology at Ecole Nationale Veterinaire d'Alfort.

Principal Investigators	**Momoh Mambu, PhD, Kenema Government Hospital** **Nell Bond, PhD, Tulane University**
Title	***Cellular immune responses to rVSVDG-ZEBOV-GP vaccination in Ebola survivors in eastern Sierra Leone***
Pathogen Focus	Filoviruses
Country	Sierra Leone
Collaborating CREID Research Centers	WAC-EID, WARN-ID, CREID-ECA, CREATE-NEO
Abstract	The devastating 2013-2016 Ebola virus disease (EVD) outbreak in West Africa was the largest in history with over 28,000 cases and 11,000 deaths. This outbreak left a large cohort of EVD survivors, many with persistent health concerns following resolution of disease, who have since participated in research studies investigating adaptive immunity to EBOV and viral persistence. Cellular immunity studies have shown that strong, diverse, T-cell responses are associated with EBOV clearance and survival. However, EBOV persists in immunologically privileged sites in survivors much longer than initially thought: the recent outbreak in Guinea was traced back to an EVD survivor who had no known exposure over five years after recovery. Recent reports suggest that EBOV IgG levels cycle within survivors over time, which suggests a potential role for periodic exposure to antigen sequestered in immunologically privileged sites. These data suggest significant risk for recurrent disease as natural immunity wanes over time. Given these risks, it is imperative to identify methods to improve EBOV specific immune responses in survivors and prevent such events from occurring in the future. Immunization of EVD survivors with the rVSVΔG-ZEBOV-GP vaccine is one such strategy. In this Pilot Program study, Drs. Momoh and Bond will leverage a unique cohort of vaccinated EVD survivors and naive, vaccinated controls to understand the role of vaccination on the strength, quality, and durability of EBOV specific cellular and systems level humoral immune responses in this population. This study will lay the groundwork for developing improved strategies for protecting EVD survivors and their communities from recurrent disease. Dr. Momoh is a scientist in the Viral Hemorrhagic Fever Research Lab at Kenema Government Hospital and Dr. Bond is a post-doctoral research fellow in Microbiology and Immunology at Tulane School of Medicine. They will be mentored by researchers with complementary expertise in immunology and vaccinology, clinical trials, immunity assays, and bioinformatics from four CREID Research Centers representing three different institutions, including UTMB, Washington State University, and Tulane School of Medicine.

Principal Investigators	**Maria Martin, PhD, and Carina Sen, MSc** **Instituto Nacional de Enfermedades Virales Humanas**
Title	***Pathogenic Mammarenaviruses and Orthohantaviruses in Argentina***
Pathogen Focus	Arenaviruses, Hantaviruses
Country	Argentina
Collaborating CREID Research Centers	WAC-EID, CREATE-NEO
Abstract	Argentina is an endemic area for several highly pathogenic roboviruses including Junin virus (JUNV), the causative agent of Argentine Hemorrhagic Fever (AHF) and several hantavirus cardiopulmonary syndromes (HCPS) causing hantaviruses. This research project will investigate two recent developments related to the rodent reservoirs of JUNV and a novel hantavirus recently identified. Since the emergence of AHF, a progressive geographic shift of epidemic outbreak epicenters has been observed. Several hypotheses have been considered to explain the geographic change of the endemo-epidemic area and changing incidence of AHF. In this Project, Dr. Martin and Ms. Sen will use historical samples from rodent collections, positive or negative for Junin virus, to investigate phylogenetic relationships between *Calomys musculinus*, the reservoir of JUNV, in endemic and extra-endemic regions of Argentina. Instituto Nacional de Enfermedades Virales Humanas (INEVH) has led studies on reservoir eco-epidemiology, laboratory diagnosis, genotype identification, and outbreak assistance for these viruses. During 2021, two new genotypes were detected in Argentina from HCPS cases. These genotypes come from areas where HCPS virus circulation has not been described. The rodent reservoirs of these genotypes remain unknown. Dr. Martin and Ms. Sen will identify the rodent reservoir of the two new genotypes by employing NextGen Sequencing of banked and fresh rodent samples. Results from the study will help elucidate the reservoir host relationships with two highly pathogenic rodent borne viruses in Argentina which may help with development of targeted public health interventions for JUNV and HCPS viruses. Dr. Maria Laura Martin, Co-PI, is a Professional Assistant with the Reservoirs and Vectors Division with INEVH in Argentina and Ms. Carina Sen, Co-PI, is an Associate Professional in the Biotechnology and Bioinformatics Division with INEVH. Dr. Martin and Ms. Sen will be co-mentored by an international, multidisciplinary team six people who are virologists, ecologists, molecular biologists, and biostatisticians and are members of two CREID Research Centers – WAC-EID and CREATE-NEO – and a senior scientific administrator from their host country of Argentina.