# 2019 MP3 Seed Grant Awardees

**Project Title**: The sum of the parts: Understanding the interaction between individual and population immunity to dengue, viral diversity, and transmission dynamics.

**Research Team**:
Matthew Collins, MD, PhD (PI; Ast Professor; SOM)
Anne Piantadosi, MD, PhD (Ast Professor; SOM)
Gonzalo Vazquez-Prokopec, PhD (Asc Professor; ECAS)

**Award Total**: $250,000 over 2 years

**Abstract**: This project leverages existing and newly generated data on virus, vector, and host in the frame of Ecological Immunology to comprehensively define dengue virus transmission dynamics. Viruses circulating in mosquito and humans over the time span of a decade will be characterized by next generation sequencing and phylogenetics. Simultaneously, neutralizing antibody responses will be defined at individual and population levels. Results will be integrated with existing epidemiologic data to generate a dengue susceptibility map that predicts novel strain introduction. The model will be validated by historical and prospective dengue surveillance, providing an invaluable tool for high priority public health activities.

**Project Title**: Microbiome organisms and natural immunity against pneumococcal disease.

**Research Team**:
Cynthia G. Whitney, MD (Professor, RSPH)
Nadine Rouphael, MD (Asc Professor, SOM)
Jesse J. Waggoner, MD (Ast Professor, SOM)

**Award Total**: $250,000 over 2 years

**Abstract:** Pneumococcal disease is a leading cause of illness and death, especially among the elderly in all countries and young children in low-income settings. How humans develop natural immunity to the range of pneumococcal serotypes is unknown. We plan to evaluate whether the presence of encapsulated Streptococcal bacteria that are part of the upper respiratory tract microbiome is associated with antibodies that could protect against invasive pneumococcal strains. If so, these commensal organisms could boost vaccine-induced or natural immunity in highly vulnerable populations, such as those in sub-Saharan Africa, where pneumococcal disease is not well controlled in spite of immunization programs.

# 2020 MP3 COVID-19 Cycle 1 Awardees

**Project Title**: Development of 2019-nCov-specific antibodies from lampreys.

**Research Team**:
Max D. Cooper, MD (Professor, SOM)
Masayuki Hirano, PhD (Ast Professor, SOM)
Balwan Singh, PhD (PI, CDC)

**Award Total**: $123,806 over 1 year

**Abstract**: The outbreak of a novel coronavirus (2019-nCoV, now also called severe acute respiratory syndromecoronavirus 2 (SARS-CoV-2)) represents a pandemic threat that has been declared a public health emergency. The coronavirus Spike (S) glycoproteins (CoV S) promote infection by fusing the viral and cellular membranes. Widely available immunoglobulin-based monoclonal antibodies (mAbs), which are specific to SARS-CoV S, do not bind to 2019-nCoV S, suggesting antibody cross-reactivity may be limited. We will generate lamprey mAbs, which are composed of Leucine-rich repeat modules, with exquisite specificity for 2019-nCov S.

**Project Title**: Landscape of coronavirus recombination acrossscales.

**Research Team**:
Anice Lowen, PhD (Asc Professor, SOM)
Mehul Suthar, PhD (Ast Professor, SOM)
Katia Koelle, PhD (Asc Professor, ECAS)

**Award Total**: $150,000 over 1 year

**Abstract**: Recombination of coronavirus genomes has been observed both in vitro and in naturally circulating viruses. This type of genetic exchange can have major implications at the population level because genetic diversity generated during this exchange expands viral adaptive potential. With the goal of anticipating epidemiologically significant recombination events involving SARS-CoV-2, we will use experimental, modeling, and phylogenetic analysis approaches to quantitatively examine recombination of human coronaviruses at cellular and population level scales. By integrating our findings across these scales, our overall objective is to identify genomic signatures of recombination that are likely to be adaptive for this family ofviruses.

**Project Title**: SARS-C0V-2 pathogenesis, immune responses, and treatment: from macaques to humans.

**Research Team**:
Mirko Paiardini, PhD (Asc Professor; Yerkes/SOM)
Anne Piantadosi, MD, PhD (Ast Professor, SOM)
Raymond Schinazi, PhD (Professor, SOM)

**Award Total**: $150,000 over 1 year

**Abstract**: This project leverages a novel model of SARS-CoV-2 infection to characterize the immune response to the virus; define the main anatomical sites and kinetics of viral replication and evolution; and test novel strategies targeted at SARS-CoV-2 that could be directly translatable to the clinic. These analyses will be performed utilizing a cross-scales approach, from cellular and molecular immunology to whole-host analysis. Simultaneously, the non- human primate data will be coupled with data generated from human specimens to understand intrahost and population level viral evolution. These results will be integrated to generate novel insights to inform the direct care of infected individuals.

# 2020 MP3 Seed Grant Awardees

**Project Title**: Characterizing the extent and epidemiological impact of hybrid schistosomes in Tanzania.

**Research Team**:
David Civitello, PhD (Ast Prof, ECAS)
Matthew Freeman, PhD; (Asc Prof, RSPH)

**Award Total**: $199,720 over 2 years

**Abstract**: Human schistosomes, blood flukes transmitted via freshwater snails, impose major, yet neglected human morbidity globally. Transmission occurs in ecologically complex communities and anintegrative multiscale approach is needed to evaluate the drivers of transmission, develop tools for surveillance, and disrupt transmission. Recent documentation of naturally occurring hybrid schistosomes, arising from cattle- and human- specialists, overturns conventional wisdom and challenges existing control measures. Hybrids are more virulent and infectious than the parental species and can backcross and persist in humans. We will characterize the prevalence and distribution of human-cattle hybrid schistosomes, identify their drivers, and assess their relevance for schistosome eradication.

**Project Title:** Integration of human contact and mobility data with infection history for models of infectious disease transmission.

**Research Team**:
Benjamin Lopman, PhD (Prof, RSPH)
Ymir Vigfusson, PhD (Ast Prof, ECAS)
Jan Vinjé, PhD, (CDC)
Kristin Nelson, PhD (Ast Prof, RSPH)

**Award Total**: $250,000 over 2 years

**Abstract**: Patterns of human contact in households, in communities, and across regions determine how infectious diseases spread and modulate the impact of control measures. However, our understanding of how human contact and mobility shape disease risk is limited. Our goal is to develop a new platform that will integrate human contact and mobility data with infection history to build tractable, realistic models of disease transmission. We will demonstrate the range and utility of this platform by modeling (1) geographic variation in rotavirus incidence post-vaccine introduction and (2) social distancing and travel restrictions to reduce spread of SARS-CoV-2.

**Project Title:** The role of macrophages in HIV transmission, persistence, and viral rebound post antiretroviral therapy interruption.

**Research Team**:
Matthew Parsons, PhD (Ast Prof; SOM)
Mirko Paiardini, PhD (Asc Prof, SOM)
Janet McNicholl, MD (CDC)

**Award Total**: $250,000 over 2 years

**Abstract**: HIV primarily infects CD4+ T-cells, but also infects macrophages. An understanding of the role of macrophages in HIV transmission and persistence will assist HIV vaccine and cure design. The proposed experiments use macaque SIV models of HIV exposure and persistence to assess the role of macrophages in HIV transmission, persistence during antiretroviral therapy (ART) and post-ART viral rebound. We will assess: (I) macrophage-mediated HIV transmission in the presence or absence of rectal syphilis; and (II) if latently infected macrophages reinitiate viral replication following ART cessation. Generated data will inform strategies to reduce HIV incidence through viral eradication and preventing transmission.

# 2020 MP3 Seed Grant Awardees (continued)

**Project Title**: Fecal Microbiota Transplantation for Multi-Drug Resistant Organism Eradication in Patients & Their Environment.

**Research Team**:
Michael Woodworth, MD (Ast Prof, SOM)
Colleen Kraft, MD (Asc Prof, SOM)
Max Lau, PhD (Ast Prof, RSPH)

**Award Total**: $200,000 over 2 years

**Abstract**: Antimicrobial resistance is an urgent threat with few effective treatments. Small, observational studies show that fecal microbiota transplantation (FMT) is up to 87.5% effective in eradicating multi-drug resistant organism (MDRO) colonization. FMT shows enormous potential as an approach to eradicate MDROs, but its mechanisms are poorly understood and its potential to reduce transmission have never been studied. This application builds a new collaboration between the Schools of Medicine and Public Health with a phase 1 trial of FMT for MDRO decolonization. This knowledge will serve as a springboard to understand mechanisms of FMT to interrupt MDRO transmission in populations.

**Project Title**: Characterizing molecular regulation of Acinetobacter baumannii phenotypes to understand its spread dynamics in a host community.

**Research Team**:
Minsu Kim, PhD (Asc Prof, ECAS) Phil
Rather, PhD (Prof, SOM)
Daniel Weissman, PhD (Ast Prof, ECAS)
Nic Vega, PhD (Ast Prof, ECAS)

**Award Total**: $300,000 over 2 years

**Abstract**: Acinetobacter baumannii is responsible for numerous outbreaks across the globe. Recently, it emerged as one of the most serious threats due to the prevalence of antibiotic resistance. We found that A. baumannii displays two different phenotypes specialized in host colonization and environmental persistence, respectively. The objective is to uncover how this pathogen regulates its phenotypes to spread in a host community. This objective will be pursued by using molecular genetics, single-cell fluorescence microscopy, high-throughput flow cytometry measurements of infection, and mathematical multi-scale modeling. The long-term goal of our studies is to manipulate phenotypic switching to control A. baumannii infections.

# MP3 COVID-19 Cycle 2 Awardees

**Project Title:** Structure, function, and rational inhibitor design of the SARS-CoV-2 RNA polymerase.

**Research Team:**
Bo Liang (Ast Prof, SOM)
Baek Kim (Prof, SOM)
Dennis Liotta (Prof, ECAS)

**Award Total**: $150,000 over 1 year

**Abstract**: The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has created a global health threat, and no vaccines or therapeutic agents are available. Viral polymerases have been major anti-viral therapeutic targets, as seen in multiple drug discovery successes. Drug design relies heavily on obtaining accurate structural and functional analysis. We will use existing, as well as our newly generated structural data to rationally design novel inhibitors optimized for the SARS-CoV-2 polymerase.

# MP3 COVID-19 Cycle 3 (co-fund with CURE) Awardees

**Project Title:** Estimating the cumulative incidence of SARS-CoV-2 infection in 50 U.S. states to inform COVID-19 vaccine evaluation.

**Research Team:**
Benjamin Lopman, PhD (Prof, RSPH)
Kayhoko Shioda, DVM/PhD (Staff Sci, RSPH)
Mannish Patel, (PI, CDC)
Matthew Collins, MD/PhD (Asc Prof, SOM)

**Award Total**: $50,000 over 1 year

**Abstract**: To understand and control the COVID-19 pandemic, we need to reliably estimate the true number of infections, i.e. the cumulative incidence. Although serology tests can identify previous infections, immunoglobulins targeting SARS-CoV-2 wane below the detectable level of serological assays over time, likely leading to underestimation of cumulative incidence. Therefore, our multidisciplinary team of Emory investigators, in collaboration with CDC, will estimate the cumulative incidence from longitudinal seroprevalence data, accounting for antibody waning. We will then estimate how the total effectiveness of COVID-19 vaccines varies depending on the baseline cumulative incidence (an estimate of population immunity) across states.

**Project Title:** Assessing breadth of infection- and vaccine-elicited immunity against emergent SARS-CoV-2 variants.

**Research Team:**
Erin Scherer, PhD (Ast Prof, SOM
Nadine Rouphael, MD (Prof, SOM)

**Award Total**: $50,000 over 1 year

**Abstract**: Three SARS-CoV-2 variants have emerged: B.1.351, B.1.1.7, and P.1. B.1.351 and B.1.1.7 are concerning because they have mutations in neutralizing antibody epitopes and are resistant to neutralization by convalescent plasma and vaccinee antibodies. We aim to determine whether P.1 is resistant to pre-variant COVID-19 patient and vaccinee antibody recognition to understand SARS-CoV-2 epitopes under selection pressure and help guide vaccine design. We also aim to assess whether memory B cells and memory helper T cells in pre-variant COVID-19 patients or vaccinees recognize variants to understand if they may play a role in the control of viral variants and disease prevention/attenuation.

# 2021 MP3 Seed Grant Awardees

**Project Title:** Dissecting the evolutionary dynamics of influenza A virus within and between naturally infected swine.

**Research Team:**
Katia Koelle, PhD (Asc Prof, ECAS)
Anice Lowen, PhD (Asc Prof, SOM)
Max Lau, PhD (Ast Professor, RSPH)

**Award Total**: $250,000 over 2 years

**Abstract**: Pigs play a clear role as 'mixing vessels' in influenza A virus (IAV) biology, allowing coinfection with distinct strains and subsequent genetic exchange through reassortment. Nevertheless, little is known about why pigs play this role so effectively. Examination of IAV evolution across biological scales is needed to assess whether (and how) pigs provide a context in which reassortant IAVs thrive. We propose to examine an individual outbreak in which IAVs of two subtypes spread through pigs at a week-long agricultural fair. We will characterize viral diversity and identify the evolutionary processes active at and across within-host, between-host and population levels.

**Project Title:** Cystic fibrosis trait carrier advantage: protecting against ancient and modern epidemics.

**Research Team:**
Rabindra Tirouvanziam, PhD (Asc Prof, SOM)
John Lindo, PhD (Ast Prof, ECAS)
Lance Waller, PhD (Prof, RSPH)
Christopher LaRock, PhD (Ast Prof, SOM)
Edward Mocarski, MD, (Prof, SOM)
Nael McCarty, PhD, (Prof, SOM)

**Award Total**: $300,000 over 2 years

**Abstract**: Yersinia pestis and Bordetella pertussis, the agents of plague and whooping cough, respectively, carry grim records of disease and death. Here, we propose the innovative idea that both these cAMP-inducing bacteria exploit the cAMP-activated CFTR channel in host cells to flush the airway mucus and delay immune recognition. Furthermore, we propose that CFTR mutations (despite causing the fatal disease cystic fibrosis when affecting both alleles) may have been selected because they endow carriers (those with one mutated allele) with resistance to plague and pertussis. This multi-scale project will explore the broad genetic, anthropological, immunological and therapeutic implications of this idea.

# MP3 co-fund with Synergy II Nexus Awards

**Project Title:** Mapping the eco-evolutionary landscape of antibiotic resistance and virulence in the bacterial pathogen Staphylococcus aureus.

**Research Team:**
Daniel Weissman, PhD (Ast Prof, ECAS)
Tim Read, PhD (Prof SOM)

**Award Total**: $50,000 over 1 year

**Abstract**: Staphylococcus aureus is a major antibiotic-resistant human pathogen. Public sequence efforts have produced > 70,000 genome sequences and it is present in many thousands of microbiome samples. We will combine the PI's expertise in population biology and the co-PI's expertise in microbial bioinformatics to develop novel analytic approaches to find genetic interactions related to the evolution of antibiotic resistance and test whether these interactions are mediated by environmental context.