Pathogen Genomic Surveillance and Immunology in Asia

Grand Challenges Global Call-to-Action

Request for Proposals

Applications due no later than Dec 16, 2022, 11:30 a.m. U.S. Pacific Time

Background

Pathogen Genomic Surveillance (PGS) can provide information about pathogen evolution and insight into the genetic basis of changes in virulence or resistance to interventions. During the COVID-19 pandemic, genomic surveillance for SARS-CoV-2 was established by many countries, including countries in Asia. It may be possible to leverage this capacity for genomic surveillance of priority endemic or epidemic pathogens. Research studies in the region have used pathogen genomics to understand transmission of particular pathogens such as dengue, *Salmonella* Typhi, and *V. cholerae.* Public labs and institutes may now be able to incorporate routine genomic surveillance of priority pathogens into their surveillance systems. It may also be valuable to build on SARS-CoV-2 genomic surveillance systems to further develop in-country capacity for the rapid immunological evaluation of SARS-CoV-2 variants of concern.

The Challenge

In response to this request for proposals, we seek projects from investigators in South and Southeast Asia that address one or both of the following two goals:

1. **Asia Pathogen Genomics Initiative (Asia PGI)**: Design and pilot a genomic surveillance program for a priority pathogen (other than SARS-CoV-2)
2. **Global Immunology and Immune Sequencing for Epidemic Response (GIISER) – Asia**: Develop capacity for immune characterization of SARS-CoV-2 variants to inform Epidemic Response

Across both goals, training of local scientists by collaborators willing and able to share knowledge and tools will create the necessary capabilities. A long-term goal is to establish a sustainable, local infrastructure that can be activated to respond to any new emerging pathogen locally and strengthen connections and collaborations between sites and with international decision-making bodies.

Funding Level: Up to 300,000 USD per year for each project, with a grant term of up to 2 years depending on the scope of the project. An additional 300,000 USD may be added to the second year budget if a proposed project includes monoclonal antibody discovery activities.

1. Asia Pathogen Genomics Initiative (Asia PGI)

Proposals are invited from country National Public Health Institutions (NPHIs) or public laboratories with links to the public health system.[1] NPHI or lab staff may propose to develop a plan for genomic surveillance of priority pathogens or syndromes and to execute a pilot surveillance program. They may identify a priority pathogen or disease/syndrome and undertake

[1] Government-funded institutes and labs that are mandated to provide surveillance data to health ministries for public health action are eligible to apply. This may include public health labs at the state or provincial level.

surveillance, and may propose staff training in the appropriate epidemiological methods, genomic technologies and bioinformatic tools to develop capability and expertise in viral, bacterial, parasite genomics, or metagenomics. In a two-year period, staff should have developed the ability to plan and conduct genomic surveillance for the chosen priority pathogen and have piloted a genomic surveillance system for the pathogen. Such a pilot system may inform surveillance scale-up or the design of molecular diagnostics for pathogens discovered using metagenomics.

Specifically, we seek proposals from NPHIs or public labs to dedicate staff to developing a pathogen genomic surveillance program by spending 2 years working on the identified objectives. This may include collaboration or placement with an expert for 1-3 months to gain training and expertise. It is the proposing organization's responsibility to identify collaborators or training institutes as needed. Budgets may include NPHI staff salary, reagents and supplies (which may be donated in kind by manufacturers), and training costs at the institution where the staff member may gain expertise.

The **objectives** for Asia PGI are:

a. To establish routine pathogen genomic surveillance to understand the epidemiology and transmission of a priority pathogen (other than SARS-CoV-2)
b. To use pathogen genomics in the public health response—including field epidemiology response—to investigate potential evolution of a priority pathogen and its impact on the epidemiology of disease
c. To use pathogen genomics to monitor the impact of vaccine introduction on the transmission dynamics or AMR characteristics of pathogen lineages causing disease.
d. To use pathogen genomics to inform the development of diagnostics and/or therapeutics.

Proposals addressing diseases affecting underserved or socioeconomically disadvantaged populations are encouraged. Surveillance focused on regions suspected to be the source for outbreak pathogens are encouraged.

Selected sites will be networked via regular symposia and meetings to ensure that knowledge and learnings are shared in the region.

2. **Global Immunology and Immune Sequencing for Epidemic Response (GIISER) - Asia**

We invite proposals to increase the in-country capacity for rapid immunological evaluation of SARS-CoV-2 variants in South and Southeast Asia. We would also consider proposals that include other pathogens of global health importance, in addition to SARS-CoV-2. Selected sites would be linked to the existing GIISER program, which was initiated in October of 2021 with 8 sites, located in Uganda, South Africa, Senegal, Nigeria, Kenya, Ghana, India, and Brazil. Points of connection could include standard protocols, bioinformatics pipelines, data sharing meetings, and training opportunities. The goal of the GIISER program is to strengthen local immunological evaluation of pathogens of epidemic importance in order to inform and impact local and global equitable decision making around vaccines, herd immunity, diagnostic assays, and therapeutics.

A successful GIISER site will be able to systematically produce data quantifying immune escape and cross protection for variants of local concern/interest. This will require that sites are able to leverage existing pathogen sequencing surveillance infrastructure to rapidly identify emerging SARS-CoV-2 variants, use existing clinical cohorts to obtain sera and blood cells from relevantly

infected individuals with appropriate informed consent, and perform detailed immunological characterization of sera/plasma (binding and neutralization assays), as well as single cell analytics for monoclonal antibody discovery. This information will be produced and communicated rapidly enough to inform public health decisions and policy makers within the local and international community. Care should be taken in the proposal to describe how these activities that are often siloed would be brought together.

Specifically, we seek proposals from NPHIs or their academic partners to: (1) Identify SARS-CoV-2 pathogen variants and appropriate subjects; (2) Perform sample collection, virus isolation, and B cell sorting; (3) Assess natural-infection-induced and vaccine-induced polyclonal antibody immunity to novel variants; and (4) Discover monoclonal antibodies in appropriate subjects. By the end of the first year of a two-year investment, sites should be performing all necessary binding and neutralization assays in their lab and sharing those results. By the end of the second year, sites should be able to communicate binding and neutralization results within 1-2 months of identifying a variant of local interest or concern. Sites including monoclonal antibody discovery should, by the end of year two, be able to perform single cell sequencing from B cells, repertoire analysis for selection of heavy + light chain pairs for subsequent expression and in vitro screening assays, small scale production of selected high quality mAbs from cDNA sequence, and screening of mAbs for binding to a variety of spike proteins, including epitope mapping.

The objectives for GIISER-Asia are:

a. Identify SARS-CoV-2 pathogen variants and appropriate subjects
b. Sample Collection and Virus Isolation
c. Assessment of natural-infection-induced and vaccine-induced polyclonal antibody immunity to novel variants
d. Local monoclonal antibody discovery
e. Local monoclonal antibody screening
f. Develop capacity for immunological evaluation of SARS-CoV-2 variants of concern (and potentially other additional pathogens of global health importance) through project immersion and targeted training with partners
g. Sustain and further develop expertise in virology, immunology, and communication with policy makers

What We Are Looking For

1. **Asia PGI requirements**: A successful Asia PGI site will formalize a framework to identify a priority pathogen or syndrome for genomic surveillance, build on the experience of sourcing samples for SARS-CoV-2 genomic surveillance and on the genomic sequencing skills gained during the pandemic, and access the expertise of epidemiologists and clinicians with insight into the epidemiology of the chosen pathogen or syndrome. We will prioritize funding for public labs or institutes that provide surveillance data to the government to inform public health interventions. Proposals should mention other available funding for the proposed work. Pathogens that are not covered by other funding mechanisms including large international programs will be prioritized. We also encourage applicants to describe the impact of ongoing, related work at the organization/site.

   All Asia PGI proposals must:

   - Describe the framework used to prioritize the chosen pathogen or syndrome
   - Describe in brief the SARS-CoV-2 genomic surveillance system in place

- Describe how staff can immediately put to use pathogen genomic sequencing technology at your site to respond to at least one of the Asia PGI objectives listed above.
- Describe how skills will be developed in sequencing of the priority pathogen chosen
- Describe the sampling approach for obtaining specimens for genomic sequencing and how the sampling approach will be optimized to answer at least one of the objectives outlined above. In addition, describe how metadata and clinical, epidemiological, or other data will be collected and combined with the sequencing data.
- Describe how the data generated from your project will be used to inform public health decision making in your area, country and/or region in a timely manner. How will you communicate your findings and engage with stakeholders to ensure uptake and use of your findings for these public health purposes? We expect that PGS data will be shared immediately with local government health officials as well as uploaded to a standard repository for genetic data such as GISAID, NCBI, or ENA.
- Articulate how the capacity built through the proposed project will strengthen your institute's approach to using pathogen genomics for surveillance.

2. **GIISER-Asia requirements**: A successful GIISER site will have access to existing pathogen sequencing capacity and bioinformatics, access to existing cohorts or clinical infrastructure, access to existing BLS3 labs and trained virologists and immunologists with some expertise in protein reagent generation. Not every site will have everything in place, but enthusiastic, creative and collaborative groups who want to get things done are encouraged to include specific requests for the support they need to get there (training, connections, technology, etc.)

   All GIISER-Asia proposals must:
   - Describe the site's ability to link together pathogen sequencing, clinical epidemiology, and immunology to rapidly produce high-quality, interpretable and informative data on neutralization breadth and cross protection for locally identified SARS-CoV-2 variants of concern.
     - This includes, but is not limited to, outgrowth of variant SARS-CoV-2 virus in appropriate BLS3 containment labs for live virus neutralization assays. Examples of anticipated results: Cele et al Nature 2021, Moyo-Gwete et al NEJM 2021, Shen et al NEJM 2021 and Wibmer et al Nature Medicine 2021.
   - Describe how, within the first year of the grant, the GIISER site will bring all required binding and neutralization assays into their lab and communicate their results.
   - Describe how, within the second year of the grant, the GIISER site will be communicating results within 1-2 months of identifying a variant of local concern.
   - Describe how, within the second year of the grant, the GIISER site will bring in all required capabilities for monoclonal antibody discovery and screening. (Proposals without an antibody scope will still be eligible for funding under this call.)
   - Describe how the site will leverage existing local expertise, collaborate, and share data effectively with other GIISER sites and international networks

Across both goals, we will not consider funding for:

- Sequencing of extant samples or isolates will not be considered as responsive to this RFP. The proposal must include a plan for prospective genomic surveillance rather than simply genomic sequencing of existing samples.
- Funding of genomic surveillance in a setting with no experience with SARS-CoV-2 surveillance. The proposed studies must leverage equipment and/or human resource capacity that was instituted during the COVID-19 pandemic.
- GIISER-Asia sites that do not have funded pathogen genomics surveillance and existing clinical cohorts to build on for the immune characterization studies.
- Studies focused on T cell immunity and characterizing the overall immune response to SARS-CoV-2 are out of scope.