Metagenomic Next Generation Sequencing to Detect, Identify, and Characterize Pathogens

Request for Proposals

Applications due no later than January 13, 2022, 11:30 a.m. U.S. Pacific Time

Background

Next generation sequencing (NGS) has proven to be indispensable in the current SARS-CoV2 pandemic, from pathogen discovery to variant characterization to novel vaccine development in record-time. This approach to using NGS underscores the potential value of this technology and its application to many other diseases from Ebola to cholera to Pathogen X. Building upon the success of previous Bill & Melinda Gates Foundation, Chan Zuckerberg Initiative (CZI) and Chan Zuckerberg Biohub (CZ Biohub) Grand Challenges collaborations, this year's opportunity will continue to offer exceptional opportunities for capacity building, on-going mentorship and the foundations of scientific, collaborative networks to detect, identify, and characterize pathogens. The ultimate goal will be to impact infectious disease decision making and public health by empowering local scientists with gold standard knowledge, experience and access to equipment and software.

Through this Grand Challenge, the Bill and Melinda Gates Foundation and Chan Zuckerberg Initiative will jointly offer funding for 10 scientific groups to explore the identification, characterization, and context of infectious disease in LMIC settings.

The Opportunity

One of the overwhelming lessons learned from the ongoing SARS-CoV-2 pandemic, has been the importance of being able to identify existing and emerging infectious diseases efficiently, in order to more effectively address and contain outbreaks, both locally and regionally. It has never been so important for clinicians and the global health community to have access to both accurate and timely estimates of disease burden and distribution. Traditionally, summaries of these data have been manually reported by national health ministries from regional clinical data, aggregated from local health centers. Local institutions, however, face multiple challenges to accurately assess the emerging needs of their community with current toolsets. For example, most clinical tests are based on common or easily detectable pathogens previously identified, which can miss occult and/or emerging pathogens. In addition, curation of large-scale pathogen data across multiple locations/platforms is time consuming and expensive, preventing facile integration of individual patient-level diagnostic data into a larger pathogen landscape on the regional and national level.

Over the last 18 months, we have seen how, when local institutions have the capacity – both at the hardware and software level - to detect emerging infections using pathogen sequencing technology, they are able to perform near-real-time data analysis that is rapidly translated into actionable public health decision making. At the heart of the ability to pivot to pathogen-specific sequencing during the pandemic, was the successful establishment of metagenomic sequencing platforms in low- and middle-resource settings, where there have traditionally been limitations in

access or availability of the following essential components: a) equipment/reagents, b) specialized biochemical training, c) accurate reference pathogen sequence databases, and d) advanced computational analytics.

The Challenge

Recognizing barriers for adoption of next-generation sequencing in global health, the Bill & Melinda Gates Foundation has partnered with the Chan Zuckerberg Biohub and the Chan Zuckerberg Initiative to enable populations in low- and middle-resource settings to benefit from cutting-edge pathogen detection, discovery and characterization. This partnership will provide highly specialized training in biosample preparation and sequencing to technical staff from awardee global health centers. Trainees will learn to use the open-source, open-access IDseq software developed by the Chan Zuckerberg Initiative (CZI) for the global health community to upload and analyze sequencing data, among other software such as Nextstrain. The BMGF-CZ Biohub-CZI partnership will therefore aim to provide selected applicants the benefits of onsite next generation sequencing and rapid pathogen detection to better understand their local pathogen landscape. We are also specifically seeking projects that endeavor to build upon their initial locally-focused effort to contribute to future data-informed decision-making at the population level via data sharing and pathogen data comparison across sites (multi-site studies will be prioritized).

This Grand Challenges (GC) award will support travel and accommodation of grantees to San Francisco for training at the CZ Biohub, and the following items: 1) a sequencer suitable for the global health environment,[1] 2) a dedicated sequencing technician, and 3) sequencing reagents for the duration of the award. CZ Biohub and CZI training will include pilot analysis of samples from their home region during hands-on, intensive mentoring. This 2-week instructional period will include both biochemical sample preparation for sequencing and bioinformatic analysis using the IDseq software platform. Specifically, the hands-on training for bench scientists will include best practices and standards for sample processing, DNA & RNA extraction, library preparation and data analysis on the global IDseq software platform. The combination of intensive training with molecular, capital equipment, reagent, and personnel support is intended to maximize the potential for sustainable, prospective, onsite analysis of patient samples upon return to the home site.

Molecular data generated at individual global sites is intended to be linked and automatically aggregated into IDseq for referencing by all participating clinics and associated sites. This method of local sequence analysis coupled with cross-site comparison could serve as a model for a process that would eventually lead to a network of pathogen detection nodes that could provide increased global transparency into regional pathogen distribution in an accurate and timely manner, and in ultimate support of a global pathogen surveillance network.

Examples of insights could include:

1. Investigating infectious etiologies for unknown medical cases
2. Identification of new pathogens

[1] To ensure the sequencer continues to be used for purposes consistent with the foundation's charitable objectives, we may request that funded applicants other than charities, universities, and similar organizations donate any sequencer purchased with grant funds to a charity or university, after the term of the project.

3. Detection of local outbreaks
4. Characterization of the local pathogen landscape, including vector-borne diseases
5. Assessment of emerging zoonotic disease, including wildlife and domestic animal reservoir sampling
6. Detection and classification of Antimicrobial Resistance (AMR) Markers, with potential for insight into antibiotic treatment discordance
7. Data-informed healthcare and resource allocation
8. Subsequent follow-up leveraging genomic epidemiology for public health, incorporating local epidemiological data and genomic analysis

We are specifically looking for sites that believe in collaborative approaches and data sharing. Grantees will be expected to partner closely with scientists and engineers and provide feedback to help guide the cloud computing software's development. Sites will also be expected to share data and collaborate with other labs in the network.

Funding level: up to USD $200,000 for each project, with a grant term of up to 24 months depending on the scope of the project.

We will consider sites that:

- Provide a clearly scoped initial project that demonstrates why this technology will provide insights that are not currently possible.
- Have space and capacity to run samples on a basic sequencer once provided with training, reagents, sequencer, and a dedicated computer. Have consistent access to electricity and the ability to upload data via the internet to a designated cloud server at least once a day.
- Are willing to give product feedback and collaborate with an engineering team through scheduled video calls, email, or other messaging service. Are committed to open science, preprints, and data sharing.
- Already have, or can rapidly acquire, necessary IRB approval for pathogen DNA and RNA sequence sharing from patients.
- Are representative of larger geographic regions

We will not consider sites that:

- Do not articulate how they will leverage the value of next generation sequencing to impact health outcomes.
- Are interested exclusively in Whole Genome Sequencing of human samples
- Do not plan to share their pathogen data and discoveries.
- Have extremely limited internet access.
- Are limited to previously stored samples, without substantial potential for prospective sample collection.