

Overcoming Challenges in COVID-19 Translational Research

Jonathan Z. Li^a and Xu G. Yu^b, for the Massachusetts Consortium for Pathogen Readiness

^aBrigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

^bRagon Institute of MGH, MIT, and Harvard, Massachusetts General Hospital, Cambridge, MA, USA

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Summary

This perspective details the logistical and other challenges faced in starting a COVID-19 biobank as part of a collaborative effort to accelerate translational research. Barriers to COVID-19 translational research are surmountable and necessary in the effort to combat this pandemic.

Corresponding

Jonathan Li, MD

Brigham and Women's Hospital

Harvard Medical School

jl@bwh.harvard.edu

Xu Yu, MD

Ragon Institute of MGH, Harvard and MIT

Massachusetts General Hospital

xyu@mgh.harvard.edu

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Key points:

1. Harmonize research efforts to present one unifying and inclusive protocol to patients with COVID-19
2. Coordinate workflow and consent efforts closely with the Institutional Review Board given the unique challenges involved in the enrollment and consent process
3. Collaborate with clinical care providers to collect research specimens to save personal protective equipment (PPE) in patient care units
4. Schedule non-overlapping laboratory shifts when possible and follow social distancing guidelines for the sample processing team members
5. Provide dedicated laboratory PPEs and establish stringent standard operating procedures for sample processing to protect laboratory workforce

It is clear that creating strong translational research programs are key to combating the COVID-19 pandemic. By facilitating research that spans bench to bedside, translational research uses cutting edge laboratory techniques to study patient samples and quickly pivots laboratory discoveries into new therapies for our patients. Across the medical spectrum, from cancer to HIV, translational research has been critical to reaching our ultimate goal of designing new diagnostic tests, understanding the underlying mechanisms of disease processes, and establishing, improving, and advancing therapies.

As the COVID-19 outbreak reached the United States, a team of clinical, basic, and translational researchers launched the Massachusetts Consortium for Pathogen Readiness (MassCPR), an effort to catalyze collaborations and facilitate the sharing of precious clinical samples and research data across institutions. As translational virologists and immunologists, we are accustomed to overcoming barriers to obtain infectious clinical specimens for laboratory-based research studies. However, the challenges that we have faced so far in this COVID-19 pandemic setting have been unprecedented. Ominous warnings came from our colleagues from Seattle and Nebraska who were among the first in the U.S. to set up research protocols for COVID-19 patients. Even with this forewarning, the complexity of the logistic challenges that we encountered cannot be overstated. This included the difficulty of obtaining samples from very ill and highly infectious patients, shortages of personal protective equipment (PPE), an overtaxed healthcare system with breakdowns across the supply chain, and the challenges of keeping our laboratory staff safe.

Our first critical step was to obtain a commitment from our institutions and its researchers to support a single COVID-19 specimen biorepository, as part of the MassCPR effort. The creation of the MassCPR biorepository permitted us to (1)

create standardized specimen collection and processing protocols across institutions, and (2) lower burden for participants by consolidating requests for research participation. We also discovered the importance of creating a unifying consent form that could be used to obtain consent from patients with COVID-19 throughout the spectrum of their disease.

The next challenge that we faced, scarcity of PPE for our research staff, coincided and partially conflicted with the importance of saving PPE for frontline clinical personnel. We worked closely with our institutional review board for a solution for hospitalized patients in respiratory isolation, eventually developing a system to obtain witnessed verbal consent by phone or via an iPad in the hospital room. For the participants who were on a ventilator, consent was obtained from their healthcare proxies. We also collaborated with our nursing and phlebotomist colleagues who helped collect inpatient research samples during the course of the patient's clinical care, samples that included blood, respiratory specimens, urine, and stool. For outpatient specimen collection, we continued to be hampered by the lack of sufficient PPE. Despite robust communication between researchers and the Massachusetts Department of Public Health to arrange home-based community sampling, we determined that this method would not be feasible at the time due to high PPE requirements. Instead, we set-up research stations within outpatient clinics that were set up to specifically evaluate patients with respiratory symptoms and/or fever. This allowed us to collect outpatient specimens from patients with mild or moderate symptoms, who serve as reference individuals for hospitalized patients with severe disease and are critical to filter host and viral factors driving disease outcome.

We also were held back in other areas of the supply chain, including a shortage of swabs and specimen transport media. So as not to compete with clinical care needs,

we sourced swabs commonly used in Asia that we independently validated, and also used both saline and dry swab collection as alternatives to specimen transport media. We also continue to struggle with hurdles in the “expertise” supply chain, as many of our investigators are physician-scientists who are balancing the competing demands of COVID-19 clinical care and research.

The laboratory processing of these COVID-19 samples was not without its own difficulties. Our first task was to develop biosafety protocols and sample processing procedures with the help of our colleagues in the clinical microbiology laboratory as well as researchers from other institutions. To provide our laboratory staff with the required PPE to safely handle these specimens, we solicited donations of PPE from other research labs and explored ways to reuse PPE in the laboratory during periods of severe shortage, such as reusing surgical masks after a period in storage. Many of our staff did not have access to personal automobiles, so we provided bicycles to laboratory staff to minimize the reliance on public transportation and limit their contact with others. As a testament to our ability to effectively protect laboratory personnel working with COVID-19 patient samples, no occupationally-acquired SARS-CoV-2 infection has been observed among our approximately 50 laboratory team members, despite processing specimens collected at times when patients are still extremely contagious. During periods of high-level community transmission, we staggered laboratory staffing schedules after several of our laboratory members had to be quarantined due to COVID-19 exposure outside of the lab. We split the laboratory processing group into compartmentalized teams that work at different times to avoid crowding and maintain social distancing in the laboratory. This also safeguarded our ability to continue processing COVID-19 samples even if a member of the laboratory were to become sick. As we navigated these stressful times, it

became paramount to support not only the physical, but also the emotional well-being of the research staff and ensure sufficient downtime.

With the support of the leadership across institutions, clinical research staff, nursing and clinical teams, and laboratory personnel, the MassCPR has successfully collected samples from over 400 participants in just eight weeks. This is a testament not only to the multitudes of dedicated healthcare workers and researchers involved in this herculean effort, but ultimately to the study participants who have agreed to share their precious time and samples with the research community in the hope of contributing acutely to the end of this outbreak. We hope that sharing our experiences will help demonstrate that barriers to COVID-19 translational research are surmountable and spur innovative researchers and participants to join forces in the effort to combat this pandemic.

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