The Role of Shared Resources in Facilitating Human and Environmental Surveillance for SARS-CoV-2

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ABSTRACT

The University of Miami (UM) and Weill Cornell Medicine (WCM) have established a collaborative study for human and environmental surveillance of SARS-CoV-2, the virus that causes COVID-19 disease, including surface, air, and wastewater based surveillance efforts. Five shared resources at UM helped establish and are currently providing coordinated support for ongoing surveillance and research, providing a case study of how a diverse array of shared resources can work together to facilitate human and environmental surveillance for SARS-CoV-2. The shared resources involved in this effort include a group of Sylvester Comprehensive Cancer Center (SCCC) Shared Resources, including the Behavioral and Community Based Research Shared Resource, Biospecimen Shared Resource, and Onco-Genomics Shared Resource, along with the Miami Clinical and Translational Science Institute (CTSI) Biostatistics Collaboration and Consulting Core, and the Miami Center for AIDS Research (CFAR) Laboratory Sciences Core. UM has deployed an extensive human surveillance testing, tracking and tracing system to monitor students, faculty, and staff, and widespread wastewater surveillance of SARS-CoV-2 from buildings on all campuses. This surveillance includes a major hospital that is part of UM and that treats COVID-19 patients. WCM has established an international consortium for SARS-CoV-2 environmental surveillance. The goals of this UM/WCM study are to generate, optimize, standardize, and compare SARS-CoV-2 human and wastewater surveillance with various sampling, processing, detection, and analysis approaches, and to integrate wastewater data with community and hospital COVID-19 prevalence, with the aim of developing predictive models of local and community level spread of COVID-19 and also the spread of other existing and emerging pathogens. The results from this effort are currently informing public health strategies on local and community levels and may serve as a model more broadly. We present here lessons learned, current results, and future directions, with a focus on the role and impact of the shared resources.

OVERVIEW

❖ Goals

- **Use environmental surveillance of SARS-CoV-2 as an early warning system for COVID-19 and as a mapping tool for new genetic variants**
- **Implement integrated human and environmental surveillance of SARS-CoV-2**, including coordinated surface, air, and wastewater screening
- **Generate, optimize, standardize, and compare SARS-CoV-2 human and environmental surveillance** with various sampling, processing, detection, and analysis approaches
- **Integrate wastewater data with community and hospital COVID-19 prevalence, with the aim of developing predictive models** of local and community level spread of COVID-19

Administrative Organization

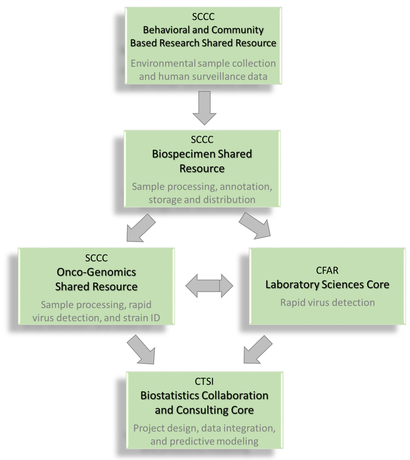
❖ Background

- Recent research on COVID-19 has found that SARS-CoV-2 can be detected in wastewater days or even a week before people show symptoms or test positive for COVID-19. To determine if environmental surveillance for the SARS-CoV-2 virus can predict COVID-19 disease outbreak, we are collecting and analyzing wastewater samples from all the University of Miami campuses. We are also analyzing wastewater samples collected from sites across the United States and around the world.
- This study is a multi-institutional collaboration between the University of Miami and Weill Cornell Medicine and also is part of an international consortium.
- University of Miami:
  - Located in Southeastern Florida, one of the hotspots of the COVID-19 pandemic.
  - Extensive human surveillance: COVID-19 testing, tracking and tracing of students, faculty, and staff. University hospital with COVID-19 patients.
  - Ongoing wastewater surveillance of SARS-CoV-2 from buildings on all of the University campuses, including student residence halls and the University hospital, since September 2020.
  - Implementing air and surface sampling, coordinated with wastewater sampling.
  - Study established with the coordinated support of 5 shared resources at UM, and the Environmental Engineering Laboratory, Institute for Data Science and Computing, Institute for Bioethics and Health Policy, Infection Control and Employee Health, Building Facilities, and Environmental Health and Safety.
- Weill Cornell Medicine:
  - Located in New York City, one of the first hotspots of the COVID-19 pandemic.
  - Established a national and international consortium for Metagenomics and Metadesign of Subways and Urban Biomes (MetaSUB), which since the start of the pandemic has focused on Metagenomics of the Sewage System (MetaSEW). This effort includes wastewater collection and analysis from a range of sites across the United States (Charlotte, Racine, New York City, Burlington, Dallas, and Los Alamos) and internationally (Kuala Lumpur, Singapore, Seoul, Shanghai, Istanbul, Marseille, Montevideo, and Buenos Aires).
  - Sequencing data generated in collaboration with the New York Genome Center and HudsonAlpha Discovery.
  - Established open-code bioinformatics platform (Pangea) for metagenomics and meta-transcriptomics analysis of human and environmental surveillance
- Innovation: Detection of SARS-CoV-2 includes the use of a novel rapid polymerase chain reaction method (V2G-qPCR) developed at UM (M. Sharkey) and a new rapid loop-mediated isothermal amplification (LAMP) method developed at WCM (C. Mason).

❖ Results are currently informing public health strategies on local and community levels

- Environmental surveillance results at UM are reported to university leadership.
- Community partners include the Miami-Dade Waste and Sewer Department and the Florida Department of Health in Miami-Dade County .

SHARED RESOURCES



Sylvester Comprehensive Cancer Center

Behavioral & Community-Based Research Shared Resource

Services:
- Coordinate recruitment and retention of study participants
- Development of culturally and linguistically tailored study materials
- Data and sample collection in clinical and community settings
- Assist development and delivery of evidence-based interventions

The BCSR facilitates behavioral, psychosocial, community, translational, and population-based research. In addition to support for cancer-focused studies, the BCSR is providing services for critical COVID-19 testing, tracking and tracing at the University and surrounding community.

Role in this study: The BCSR facilitates wastewater and surface sample collection, and facilitates access to COVID-19 population-level data from human surveillance.

Biospecimen Shared Resource

Services:
- Biospecimen collection, annotation, processing, storage and distribution
- Rapid acquisition of surgical tissue and fresh biopsies
- Plasma, serum, and PBMC processing and cryopreservation
- FFPE and frozen tissue processing, sectioning, staining, & scanning
- Participant screening and enrollment for biospecimen studies

Role in this study: The BSSR is the biorepository for the environmental samples (air, surface and wastewater) from this study and provides sample metadata annotation, tracking, processing (concentration), storage and distribution. The BSSR also provides support for basic physical chemical measurements and culture- based microbiological analyses (including analysis of E. coli) for the wastewater samples.

Onco-Genomics Shared Resource

Services:
- Next generation sequencing
- Single cell genomics
- Spatial genomics
- Digital gene expression
- Sample preparation (nucleic acid extraction and purification)

Role in this study: The OGSR receives concentrated samples from the BSSR and provides rapid RNA extraction and purification, rapid detection with RT-qPCR and LAMP, and next generation sequencing for samples that test positive for SARS-CoV-2, for strain variant ID and metagenomics.

Center for AIDS Research

Laboratory Sciences Core

Services:
- Human primary cell preparation
- Evaluation of cytokines and soluble mediators
- Flow cytometry, Luminex and ELISA services
- Cell assays and microbial marker evaluation
- Multiplex RT-qPCR
- Virology services

Role in this study: The LSC provides rapid viral detection with a novel rapid polymerase chain reaction (PCR) method developed and adapted for wastewater surveillance by a CFAR investigator (M. Sharkey).

Clinical & Translational Science Institute

Biostatistics Collaboration and Consulting Core

Services:
- Study design and statistical support for basic, translational, and clinical research
- Randomization schemes for sampling designs and group assignment
- Facilitates design of appropriate statistical analysis plans
- Sample size estimation and power analysis
- Longitudinal, multivariate, and survival analysis
- Data and database management

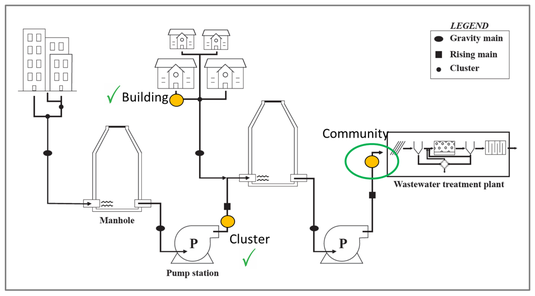
Role in this study: The BCCC provides support for developing study and experimental designs that maximize efficiency, increase interpretability and generalizability, and enhance the ethical conduct of research. The BCCC facilitates the formulation of hypotheses that are statistically testable; applies robust and efficient analytic methods to estimate effects precisely and to efficiently test significance; and helps refine measurements to increase precision and sensitivity. The BCCC is facilitating the development of COVID-19 disease predictive models that integrate human and environmental SARS-CoV-2 surveillance data.

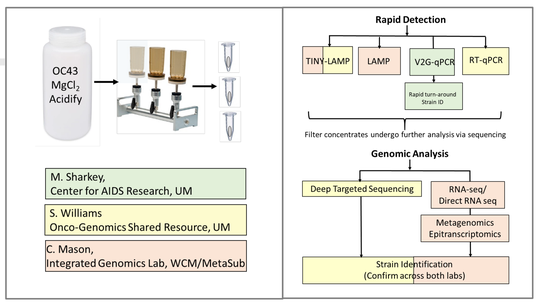
RESULTS

WASTEWATER CHARACTERIZATION

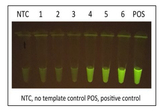
- Evaluate influence of watershed scale
- Evaluate sample concentration methods
- Evaluate sample collection method on SARS-CoV-2 measures
- Relate wastewater to human surveillance data

Electronegative filtration





A novel polymerase chain reaction method (V2G-qPCR) has been developed at UM by M. Sharkey and has been validated for SARS-CoV-2 detection with wastewater samples. V2G-qPCR combines standard PCR with a novel polymerase that can efficiently use both RNA and DNA as templates and retains polymerase activity in unprocessed biological fluids. This approach eliminates RNA extraction and cDNA synthesis steps. Positive viral RNA amplification is detected via sequence-specific fluorescent hydrolysis probes visualized at PCR endpoint by blue light excitation.

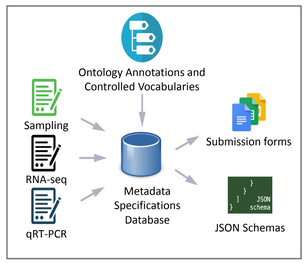


V2G-qPCR detection of SARS-CoV-2 RNA. Detection of viral RNA using previously tested (by RT-qPCR) negative (1-3) and positive (4-6) samples.

Wastewater characterization. Wastewater samples are collected in collaboration with University Facilities and Environmental Health and Safety. Samples are concentrated at the SCCC Biospecimen Shared Resource. Concentrated samples are split and sent to the SCCC Onco-Genomics Shared Resource for RT-qPCR and targeted sequencing analysis, to the CFAR Laboratories Sciences Core for V2G-qPCR analysis, and to Weill Cornell Medicine for RNA-seq, metagenomics, epitranscriptomics, and strain variant identification.

DATA STANDARDIZATION

- Establish data and metadata categories and develop metadata standards
- Establish end-to-end data flow process
- Implement operational informatics infrastructure to manage data & metadata
- Implement Data Portal for data access and integration

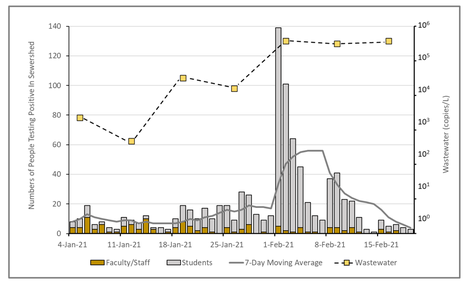


- Data and metadata categories
- Formal description
- Metadata standards management
- JSON schemas
- Submission forms

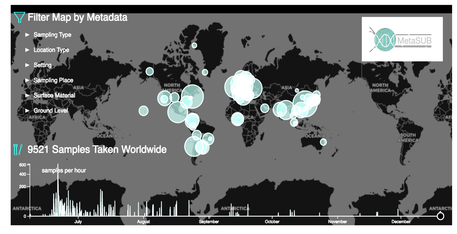
Metadata standardization and processing. Top: Formalized representations of metadata. All data fields (properties) to describe samples and datasets are formally described using reference schemas and ontologies. That includes the description of the properties themselves and their allowed values. The formalized data standards are managed in a dedicated database and made available via one or more JSON schemas that can be used to generate submission forms. Bottom: Data submission process. Forms generated based on the JSON metadata schemas are used to capture and validate required information to describe samples and datasets. The descriptions are saved in a document database (Mongo DB) in JSON-LD. From the database they are available via a REST API to end users who access a Data Portal or collaborators who access and integrate the data into other systems. The JSON-LD format formally describes the property fields and values and is machine interoperable.

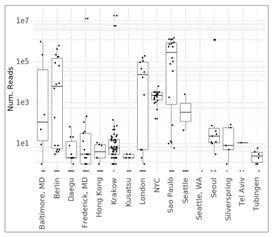
INTEGRATION OF HUMAN & ENVIRONMENTAL SURVEILLANCE

- Strain tracking and viral detection methods comparison (qPCR, LAMP, RNA-seq)
- Predictive modeling that integrates wastewater testing with local & regional health data
- Compare UM data to national and global COVID-19 strains and dynamics

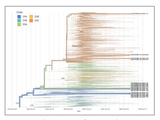


Integration of environmental and health surveillance data at a university. This chart shows the weekly SARS-CoV-2 viral load detected in wastewater over 7 consecutive weeks at defined locations on the UM campuses (dotted line) and the daily number (bars), and 7-day moving average (solid line), of faculty, staff and students from the same sewershed locations who tested positive for the virus. The wastewater viral load displays up to a 7 day lead time compared to human test data. Preliminary data indicates that this may be followed by up to a 30 day lag time (i.e., an extended time of high viral loads in wastewater), possibly due to continued virus shedding by infected individuals who stay in the area.

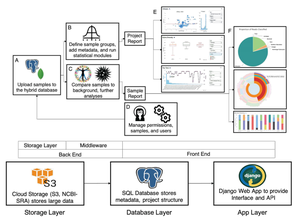




International wastewater surveillance. The map (above) and chart (left) show the range of SARS-CoV-2 viral load detected from samples collected during ongoing wastewater surveillance from 16 cities from around the world, and analyzed as part of this study.



Metagenomics and variant strains identification. Preliminary data show a wide range of species present in the environmental samples, and also shows our ability to call variants and strains even from fragmented genomes.



Data analysis and data management for this project is facilitated by Pangea, a data platform designed by team members at WCM, led by C. Mason. Pangea integrates cloud storage services with high performance computing (HPC) analysis and provides tools for project management, for data and metadata tracking, and for searching, visualizing and comparing hundreds of datasets.

Predictive modeling. Using the data from this study, we are currently building the foundation of an infectious disease model designed to anticipate outbreaks based on wastewater surveillance, human test results, clinical metadata and local hospitalization data. The results from this study will be integrated with the U.S. Centers for Disease Control and Prevention's (CDC) efforts to track emerging pathogens.

FUTURE DIRECTIONS

- Increase frequency of wastewater sampling to provide finer resolution for comparison with human surveillance cases
- Conduct hourly environmental sampling to evaluate degradation of SARS-CoV-2 signal.
- Expand phylogenetic placement of called environmental variants (NextStrain and GISAID)
- Continue data cleaning and integration, leveraging CDC and city databases, plus CVS data
- Test utility of air surveillance of virus for predictive modeling of disease
- Test mobile LAMP detection device (TINY-LAMP) for point-of-collection wastewater analysis

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