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

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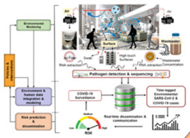
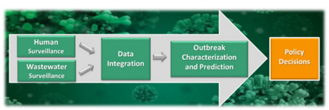
ABSTRACT

The Sylvester Comprehensive Cancer Center Shared Resources, working closely with other shared resources at the University of Miami (UM), helped establish and maintain coordinated support for a multi-institutional study on environmental monitoring of SARS-CoV-2, the virus that causes COVID-19, including surface, air, and wastewater-based sampling. This project provides a case study of how a diverse array of shared resources can work together to facilitate human and environmental pathogen surveillance. The study is a collaborative effort between researchers at UM and Weill Cornell Medicine (WCM). The shared resources involved in this project include a group of Sylvester Shared Resources, including the Behavioral and Community Based Research Shared Resource (BCSR), Biospecimen Shared Resource (BSSR), and Onco-Genomics Shared Resource (OGSR), along with the Miami Clinical and Translational Science Institute (CTSI) Biostatistics Collaboration and Consulting Core (BCCC), and the Miami Center for AIDS Research (CFAR) Laboratory Sciences Core. UM deployed an extensive human surveillance testing, tracking and tracing system to monitor students, faculty, and staff. This study extends these efforts to encompass wastewater surveillance of SARS-CoV-2 from buildings on all the UM campuses, the city of Miami and surrounding county, and UM-affiliated hospitals. The goals of this study are to generate, optimize, standardize, and compare SARS-CoV-2 human and wastewater surveillance with various sampling, processing, detection, and analysis techniques. The environmental viral surveillance data is being integrated with community and hospital COVID-19 disease prevalence, with the aim of developing predictive models of local and community level spread of the disease. The results from this effort are informing public health strategies on local and community levels and may serve as a model more broadly for other existing and emerging pathogens. 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


Administrative Leads
Helena Solo-Gabriele, George Grills, Stephan Schürer, Chris Mason
Data Standardization
Stephan Schürer, Dusica Vidovic
Wastewater Characterization
Helena Solo-Gabriele, Chris Mason
Integration with Human Health Surveillance
Chris Mason, Naresh Kumar
Human Population and Clinical Patient Surveillance
Erin Kobetz, Natasha Solle, Bhavarth Shukla

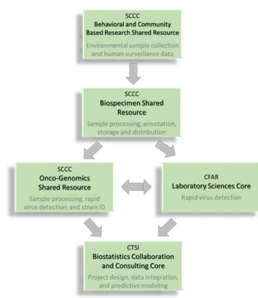
❖ **Background**

- 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 air, surface, and wastewater samples from all the University of Miami campuses plus various locations in Miami Dade County. 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 is also part of the MetaSUB international consortium.
- University of Miami:
  - Located in Southeastern Florida, one of prior 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 the University campuses, including student residence halls and the University hospital, since September 2020.
  - Implemented 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 (e.g., Charlotte, Racine, New York City, Burlington, Dallas, and Los Alamos) and internationally (e.g., Kuala Lumpur, Singapore, Seoul, Shanghai, Istanbul, Marseille, Montevideo, and Buenos Aires).
  - 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


SCCC
Behavioral and Community Based Research Shared Resource
Environmental sample collection and human surveillance data
SCCC
Biospecimen Shared Resource
Sample processing, annotation, storage and distribution
SCCC
Onco-Genomics Shared Resource
Sample processing, rapid virus detection, and strain ID
CFAR
Laboratory Sciences Core
Rapid virus detection
CTSI
Biostatistics Collaboration and Consulting Core
Project design, data integration, and predictive modeling

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 provides 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 and stores all sample metadata in a LIMS.

Onco-Genomics Shared Resource

Services:
- Next generation sequencing
- Single cell genomics
- Spatial genomics
- Molecular quantitation
- 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

Department of Public Health Service, Miller School of Medicine

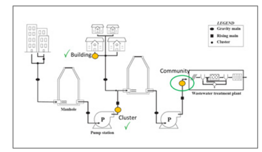
Services:
- Study design and statistical support for basic, translational, and clinical research
- Randomization schemes for sampling designs and group assignment
- Facilitates design of appropriate statistical analysis plans
- Sample size estimation and power analysis
- Longitudinal, multivariate, and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

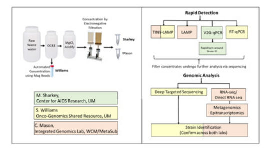
Role in this study: The BCCC provides support for developing study and experimental designs that maximize efficiency, increase interpretability and generalizability, and enhance the ethical conduct of research. The BCCC facilitates the formulation of hypotheses that are statistically testable; applies 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

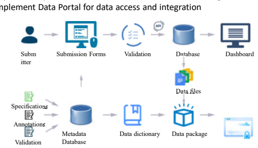



Concentration by Electronegative Filtration
Raw Waste water
OC43
MgCl2 Acidify
Sharkey
Mason
Automated Concentration using Mag Beads
Williams
M. Sharkey, Center for AIDS Research, UM
S. Williams Onco-Genomics Shared Resource, UM
C. Mason, Integrated Genomics Lab, WCM/MetaSub
Rapid Detection
TINY-LAMP
LAMP
V2G-qPCR
RT-qPCR
Rapid turn-around Strain ID
Filter concentrates undergo further analysis via sequencing
Genomic Analysis
Deep Targeted Sequencing
RNA-seq/ Direct RNA seq
Metagenomics Epitranscriptomics
Strain Identification (Confirm across both labs)

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



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. 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.

Publications

Lessons learned from SARS-CoV-2 measurements in wastewater.
Sharkey ME, et al. Sci Total Environ. 2021 Dec; 798:149177. PMID: 34375259.

A rapid, isothermal, and point-of-care system for COVID-19 diagnostics
Mozsary C, et al. J Biomol Tech. 2021 Sept; 32(3):221-227. PMID: 35136383.

Loop-mediated isothermal amplification detection of SARS-CoV-2 & myriad other applications.
Moore KJM, et al. J Biomol Tech. 2021 Sep;32(3):228-275. PMID: 35136384.

A global metagenomic map of urban microbiomes and antimicrobial resistance.
Danko D, et al. Cell. 2021 Jun;184(13):3376-3393. PMID: 34043940.

Integrating virus monitoring strategies for safe non-potable water reuse.
Jiang SC, et al. Water. 2022 Apr; 14(8):1187.

Comparison of electronegative filtration to magnetic bead-based concentration and V2G-qPCR to RT-qPCR for quantifying viral SARS-CoV-2 RNA from wastewater.
Babler KM, et al. ACS EST Water 2022 May; 2(11):2004.

Relationships between SARS-CoV-2 in wastewater and COVID-19 clinical cases and hospitalizations, with and without normalization against indicators of human waste.
Zhan Q, et al. ACS EST Water 2022 May; 2(11):1992.

Predicting COVID-19 cases using SARS-CoV-2 RNA in air, surface swab & wastewater samples.
Solo-Gabriele HM, et al. Sci Total Environ. 2023 Jan; 857(1):159188. PMID: 36202365.

Future Directions

Wastewater surveillance of COVID-19 in public schools
- Pilot project in collaboration with a RADx/UP funded investigator at the University of Miami (1OT2HD108111, Dr. Lisa Gwynn, principal investigator)

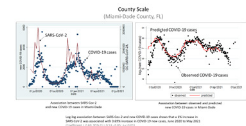
Airplane and airport wastewater surveillance
- In collaboration with the CDC-NWSS and The Rockefeller Foundation

Wastewater surveillance for influenza, for antibiotic resistant pathogens, and for other biomarkers of disease

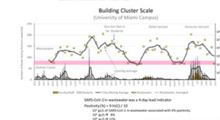
INTEGRATION OF HUMAN & ENVIRONMENTAL SURVEILLANCE

- 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

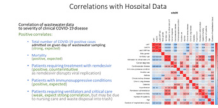
County Scale
(Miami-Dade County, FL)



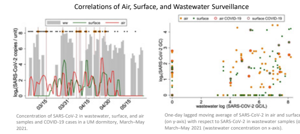
Building Cluster Scale
(University of Miami Campus)



Correlations with Hospital Data


Correlation of wastewater data to severity of clinical COVID-19 disease
Positive correlates:
Total number of COVID-19 positive cases admitted on given day of wastewater sampling (strong, expected)
Mortality (positive, expected)
Patients requiring treatment with remdesivir (positive, counterintuitive as remdesivir disrupts viral replication)
Patients with immunosuppressive conditions (positive, expected)
Patients requiring ventilators and critical care (weak, expect strong correlation, but may be due to nursing care and waste disposal into trash)

Correlations of Air, Surface, and Wastewater Surveillance



Concentration of SARS-CoV-2 in wastewater, surface, and air samples and COVID-19 cases in a UM dormitory, March–May 2021.

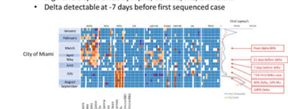
One-day lagged moving average of SARS-CoV-2 in air and surface samples (on y-axis) with respect to SARS-CoV-2 in wastewater samples (on x-axis), March–May 2021 (wastewater concentration on x-axis).

Predictive modeling. Using data from this study, we are 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. SARS-CoV-2 RNA was detected in air, surface swabs and wastewater. The relative efficiency of predicting COVID-19 cases improved to 100% when multiple environmental media were monitored (air plus wastewater or air plus surface swabs). SARS-CoV-2 was also detected in environmental samples when COVID-19 cases were not reported, indicating underreporting of COVID-19 cases. Thus, environmental monitoring of SARS-CoV-2 serves as effective method of community surveillance of COVID-19 disease.

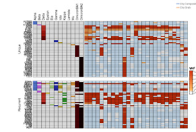
Detection of SARS-CoV2 lineages in wastewater

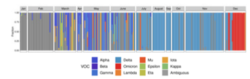
- SARS-CoV-2 lineages in City wastewater mirror patient data
- Even at low viral load lineages can be discerned
- High diversity followed by Alpha, Gamma, Mu, then Delta
- Delta detectable at -7 days before first sequenced case

City of Miami



Dynamically updating VOCs to monitor: Samples shown here include Jan/Feb 2022 along with some summer 2021 samples. Omicron BA.2 signature mutations added in January 2022.





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https://covidsfrad.org

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