

Clinical Laboratory COVID-19 Response Call

Monday, February 8th, 2021 at 3:00 PM ET

- **Welcome**
 - Jasmine Chaitram, CDC Division of Laboratory Systems (DLS)
- **CDC Virtual Reality Laboratory Training Course**
 - Joe Rothschild, CDC Division of Laboratory Systems (DLS)
- **Sequencing Efforts of Public Health Laboratories**
 - Heather Blankenship and Marty Soehnlén, Michigan Department of Health and Human Services
- **SARS-CoV-2 Variants Update**
 - Vivien Dugan, CDC Laboratory and Testing Task Force for the COVID-19 Response
- **Vaccine Breakthrough Case Investigations**
 - Leisha Nolen, CDC COVID-19 Response Vaccine Breakthrough Team
- **FDA Update**
 - Tim Stenzel, U.S. Food and Drug Administration (FDA)

COVID-19 Resources for Laboratories

- **LOINC In-Vitro Diagnostic (LIVD) Test Code Mapping for SARS-CoV-2 Tests**
<https://www.cdc.gov/csels/dls/sars-cov-2-livd-codes.html>
- **IVD Industry Connectivity Consortium**
<https://ivdconnectivity.org/livd/>
- **Antigen Testing Guidance**
<https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html>
- **Frequently Asked Questions about COVID-19 for Laboratories**
<https://www.cdc.gov/coronavirus/2019-ncov/lab/faqs.html>
- **Interim Guidance for Collecting, Handling, and Testing Clinical Specimens**
<https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html>
- **Diagnostic Tools and Virus**
<https://www.cdc.gov/coronavirus/2019-ncov/lab/tool-virus-requests.html>
- **Emergency Preparedness for Laboratory Personnel**
<https://emergency.cdc.gov/labissues/index.asp>
- **CDC Laboratory Outreach Communication System (LOCS)**
<https://www.cdc.gov/csels/dls/locs/>

CDC Preparedness Portal

<https://www.cdc.gov/csels/dls/preparedlabs/covid-19-clinical-calls.html>

Find CLCR call information, transcripts, and audio recordings on the CDC Preparedness Portal

The screenshot shows the 'Prepared Laboratories' section of the CDC website. The main heading is 'Clinical Laboratory COVID-19 Response Calls'. Below the heading is a banner image with the text 'Laboratory Professionals: Find COVID-19 information from LOCS.' and the LOCS logo. The page includes a navigation menu on the left with options like 'Preparedness Initiatives', 'Outbreak & Response', and 'Tools & Resources'. Under 'Outbreak & Response', there is a list of months from August 2020 to March 2020. The main content area contains a paragraph about the calls and a 'Participation Information' section with a 'Connect to Zoom' link.

Prepared Laboratories

Prepared Laboratories > Outbreak & Response

Preparedness Initiatives

Outbreak & Response

COVID-19

Clinical Laboratory COVID-19 Response Calls

August 2020

July 2020

June 2020

May 2020

April 2020

March 2020

Tools & Resources

Clinical Laboratory COVID-19 Response Calls

Laboratory Professionals:
Find COVID-19 information from LOCS.

LOCS
Laboratory Outreach Communications System

CDC's Division of Laboratory Systems (DLS) convenes regular calls with clinical laboratories to discuss the nation's clinical laboratory response to coronavirus disease (COVID-19). These Clinical Laboratory COVID-19 Response Calls take place every other Monday at 3:00 PM EDT. Audio and transcripts are posted online after each call.

To submit questions for consideration, email DLInquiries@cdc.gov in advance or use the question and answer (Q&A) function in Zoom during the call. Because we anticipate a large number of participants on this call, and many questions, we may not be able to directly and immediately address every issue. However, we will note your questions and feedback and tailor the content of future calls accordingly. We want this call to be useful and relevant to your COVID-19 response activities - we are all in this together.

Participation Information
[Connect to Zoom](#)

Schedule for Clinical Laboratory COVID-19 Response Calls

The next call will be on **Monday, February 22nd**
from **3:00 PM to 4:00 PM ET**



We Want to Hear From You!

Training and Workforce Development

Questions about education and training?

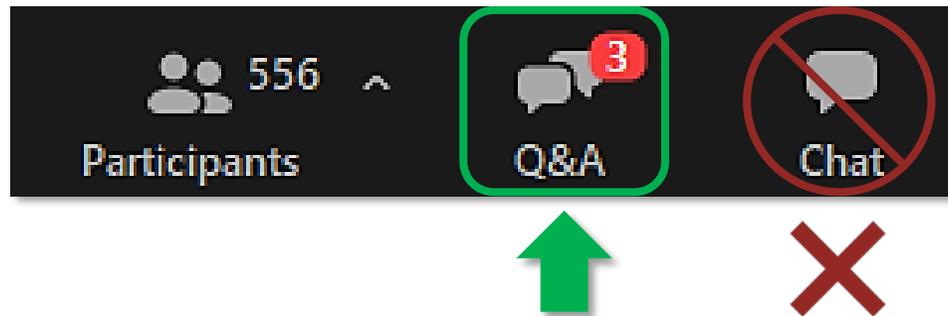
Contact LabTrainingNeeds@cdc.gov



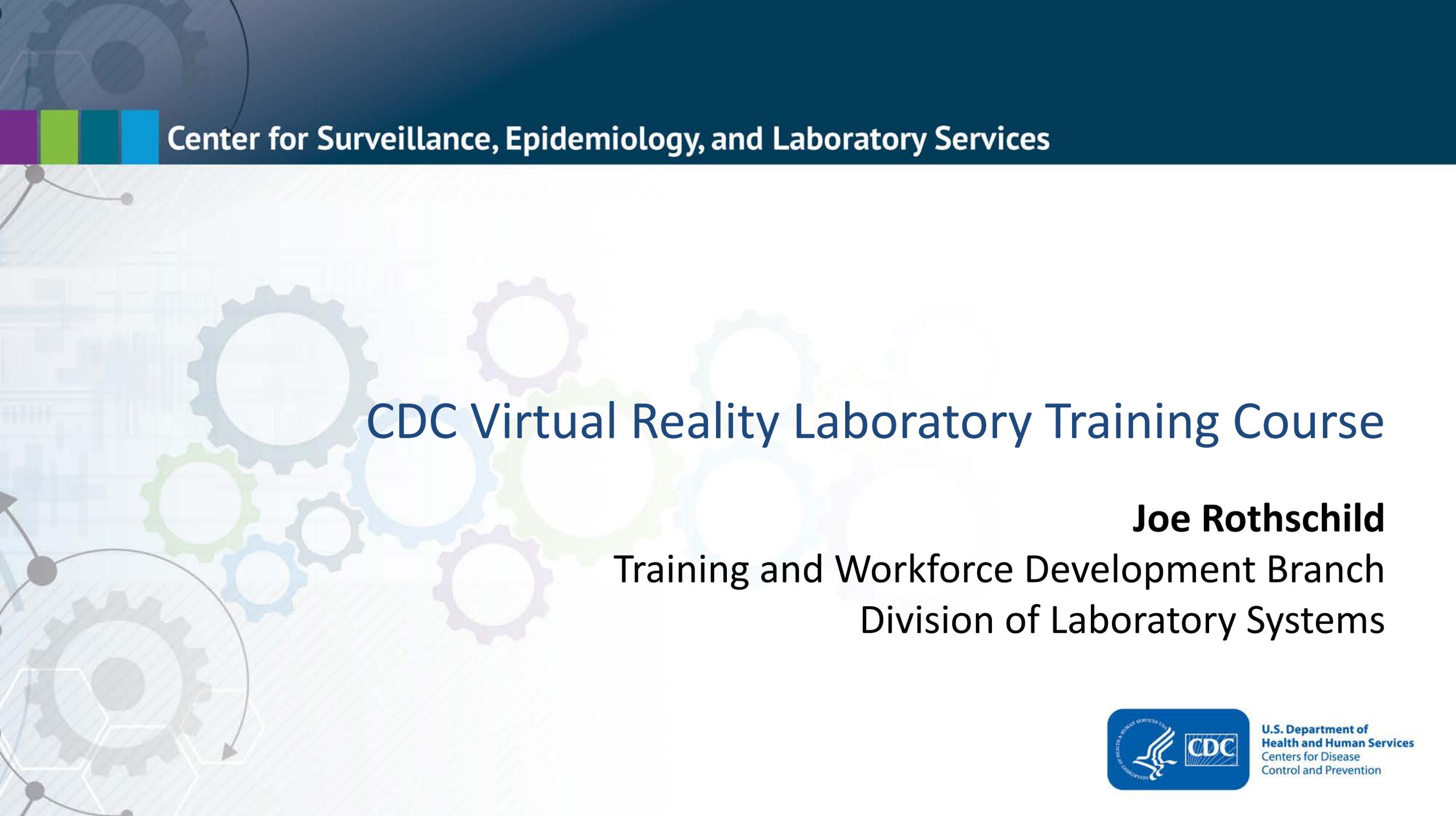
How to Ask a Question

- **Using the Zoom Webinar System**

- Click the **Q&A** button in the Zoom webinar system
- Type your question in the **Q&A** box and submit it
- **Please do not submit a question using the chat button**



- For media questions, please contact CDC Media Relations at media@cdc.gov
- If you are a patient, please direct any questions to your healthcare provider



Center for Surveillance, Epidemiology, and Laboratory Services

CDC Virtual Reality Laboratory Training Course

Joe Rothschild

Training and Workforce Development Branch
Division of Laboratory Systems



U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

UPDATED
CONTENT!



BIOSAFETY CABINET EDITION

Available on
CDC TRAIN
and



cdc.gov/labtraining



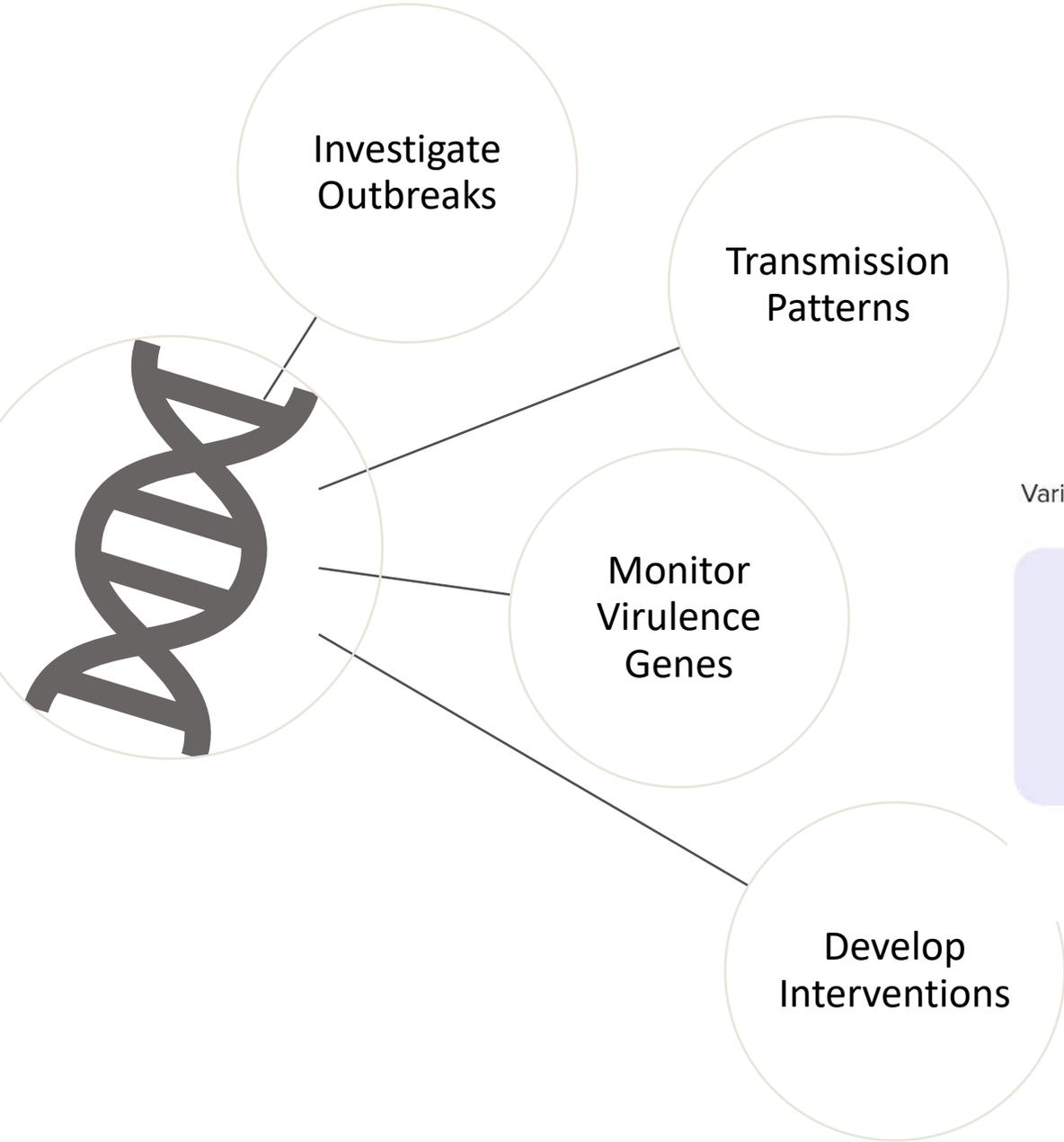
CDC DLS Presentation

8 February 2021

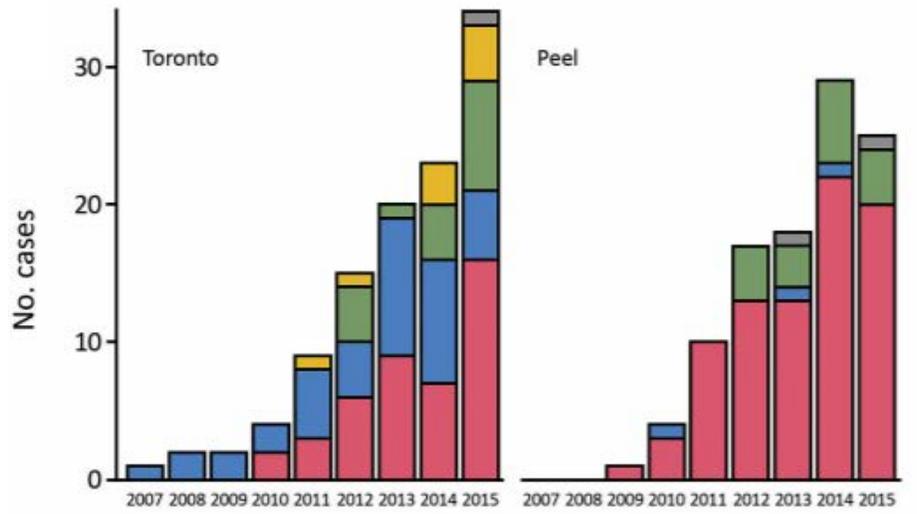
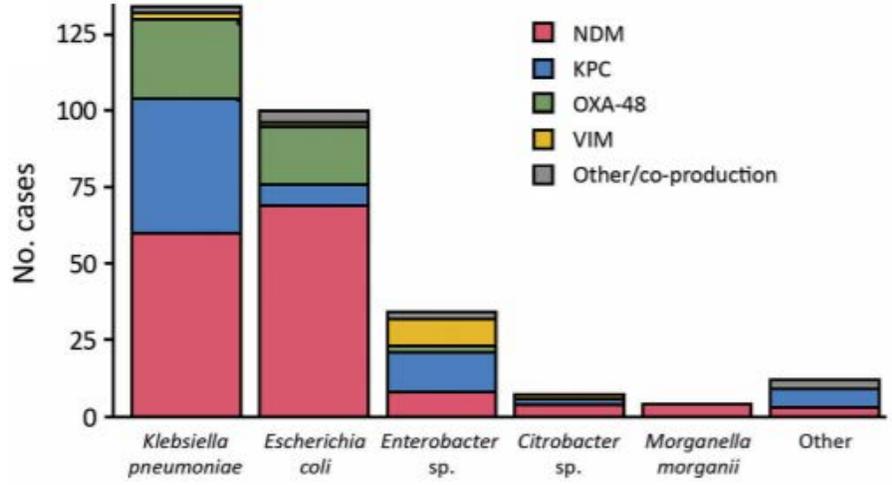
Marty Soehnlén, PhD MPH PHLD(ABB)
Director of Infectious Disease
Michigan Dept of Health and Human Services

Heather Blankenship, PhD
Bioinformatics/Sequencing Section Manager
Michigan Dept of Health and Human Services

Use of Pathogen Genomics



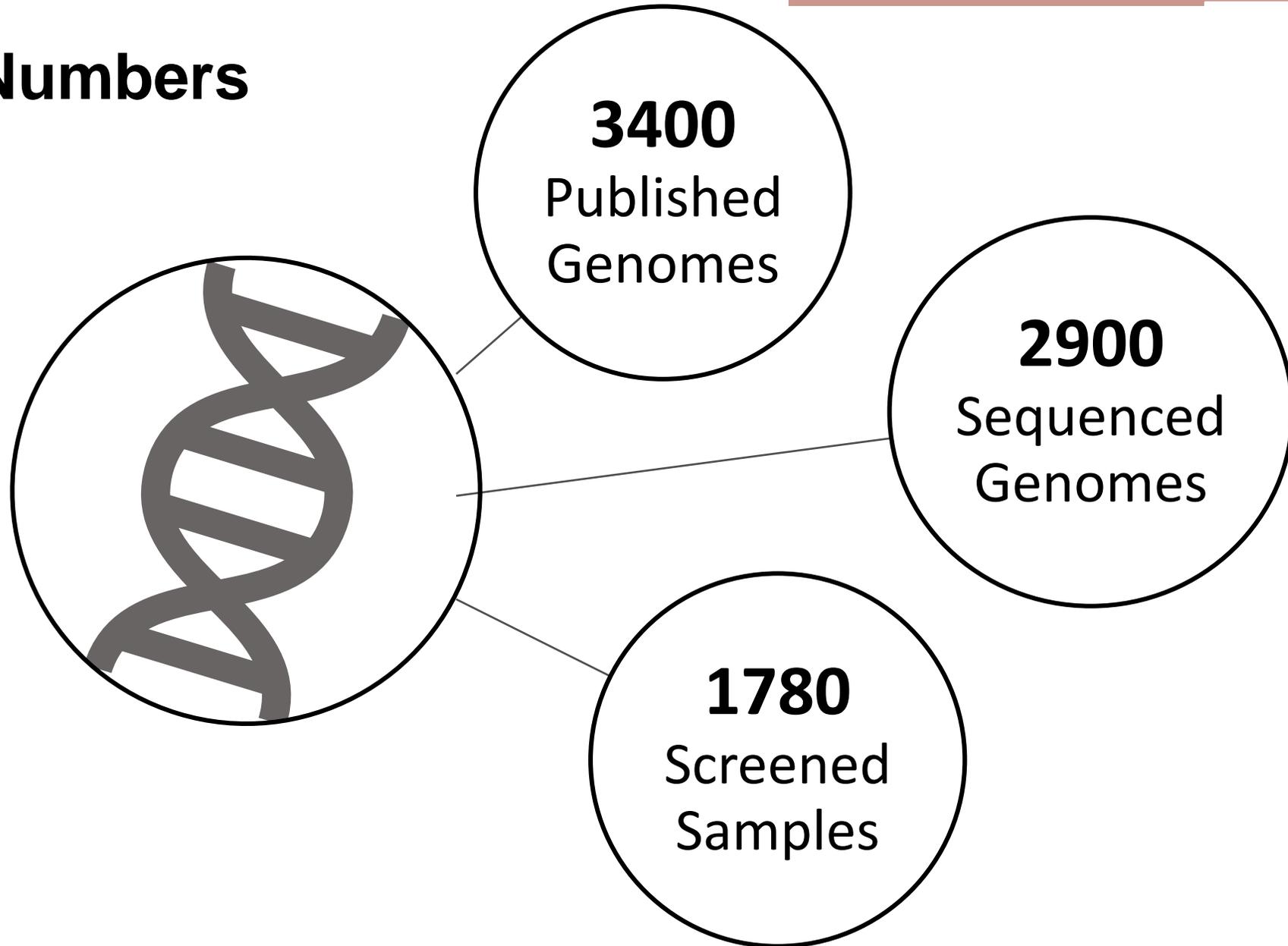
Various viral samples from patients



SARS-CoV-2 Response

- 1 Identify baselines for the virus
- 2 Examine transmission dynamics
- 3 Identify clinically important variants
- 4 Contribute to the viral biology knowledge
- 5 Examine cluster outbreaks

Current Numbers



SARS-CoV-2 Response

Sequencing

- Wet Lab
- Sequencer

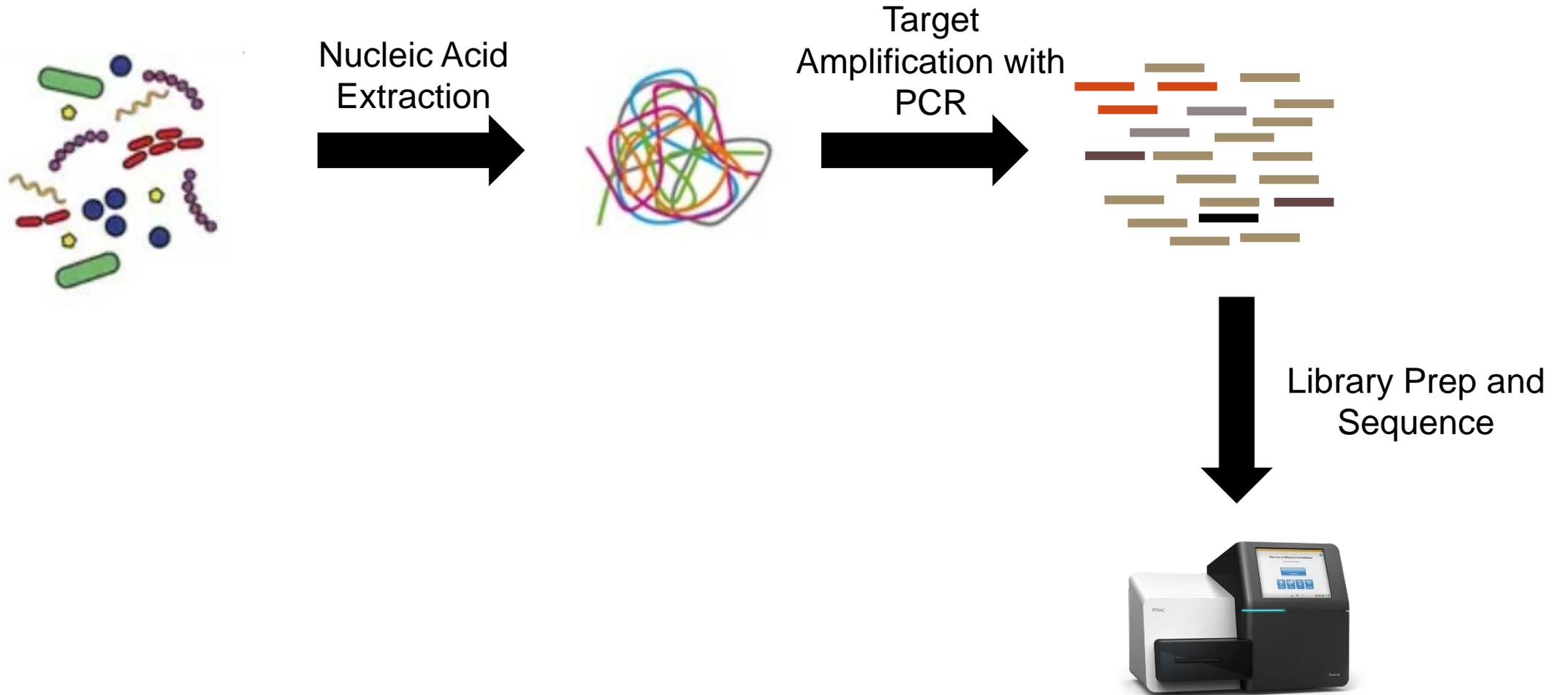
Bioinformatics

- Pipelines
- QC
- Public Repositories

Communicate

- Share with epi partners
- Nextstrain
- Visualizations

Sequencing



Nucleic Acid Extractions

- QIAGEN EZ-1
- QIAGEN QIAcube
- MagnaPure 24
- MagnaPure Compact
- ThermoFisher Kingfisher
- Omega BioTek**



No difference among
extraction methods

** by end of February

What do we sequence?

- Anything with a Ct < 30-32
 - PCR screen: CDC primers or ThermoFisher
- Epidemiological interest: within a reasonable Ct value
- Representative sample distribution

Sequencing Preps

- ARTIC v3 primers -> Nextera XT -> NextSeq
- ARTIC v3 primers -> Nextera Flex -> MiSeq
- QIAGEN QIAseq -> Nextera Flex -> MiSeq
- QIAGEN QIAseq -> Nextera XT -> NextSeq

SARS-CoV-2 Response

Sequencing

- Wet Lab
- Sequencer

Bioinformatics

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Bioinformatics

- Pipelines
 - computational space and resources available
 - command line v packages (CLC Workbench, BioNumerics, etc)
- QC
 - at what thresholds will you make for sharing data public or utilize for analysis
 - our thresholds:
 - read coverage: 50X
 - genome coverage: >94% coverage

Public Repositories

- GISAID – consensus sequence
- NCBI – raw sequencing data and/or consensus sequence
 - requires confirmation that human reads are cleaned from the data

SARS-CoV-2 Response

Sequencing

- Wet Lab
- Sequencer

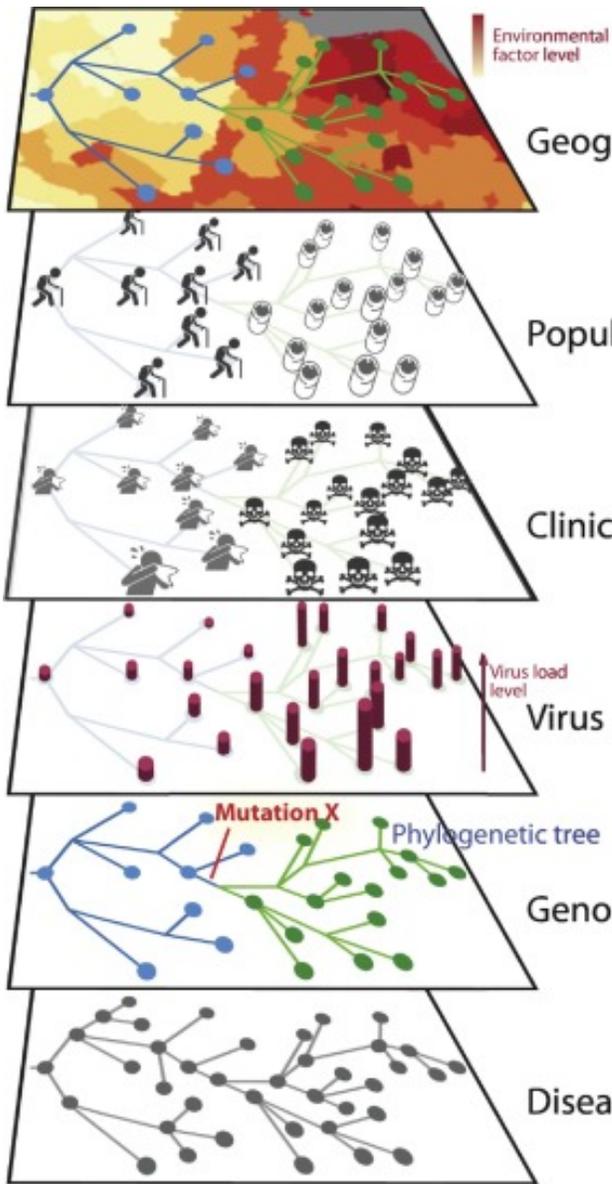
Bioinformatics

- Pipelines
- QC
- Public Repositories

Communicate

- Share with epi partners
- Nextstrain
- Visualizations

**How can we use the
data for public health
action?**



Environmental factor level

Geography/environments

Population demography

Clinical manifestation

Virus phenotype

Virus load level

Mutation X

Phylogenetic tree

Genomic sequences

Disease transmission history

Phylogenetic tree inferred from the genomic sequences serves as proxy of disease transmission history.

Examples of interpretations from the comparative analysis with the phylogeny

The emerged lineage is introduced to a certain geographic region, where some environmental factors may promote the transmission.

The emerged lineage has selective advantage in infecting and transmitting among the certain age group of host.

The emerged lineage is associated with distinctive clinical presentation/severity, which could be due to altered viral phenotype itself or the interaction with the host.

The emerged lineage exhibits a different viral phenotype such as viral shedding titer or duration, which may be due to the common mutation in the viral lineage.

Overlaying Epidemiological and Genomic Data

SARS-CoV-2 Report

Genomic Epidemiology SARS-CoV-2 in Michigan : M...

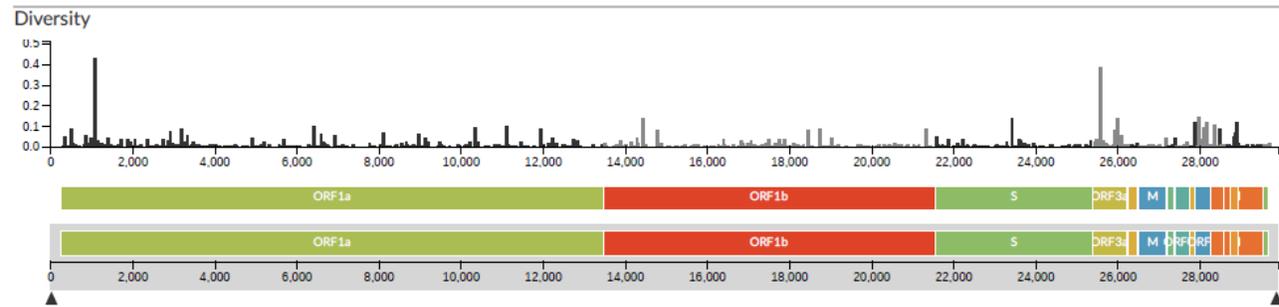
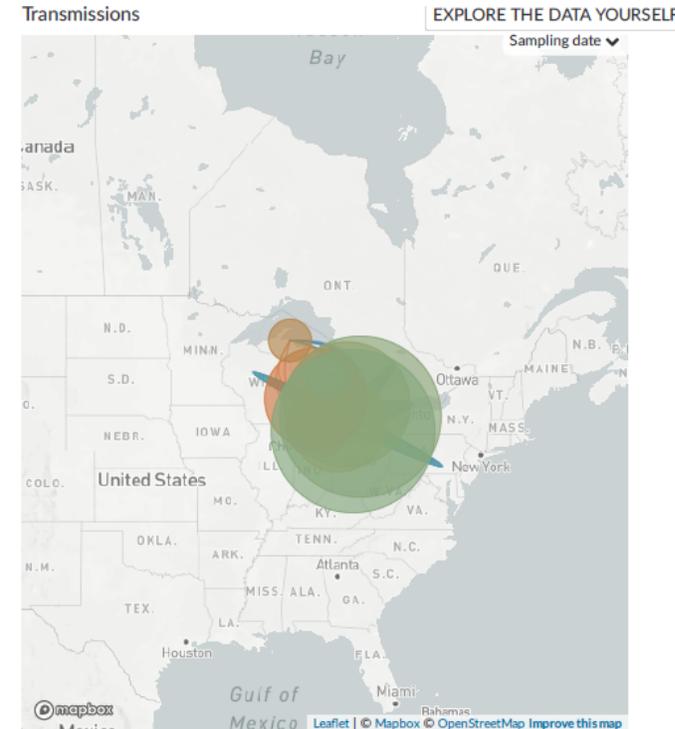
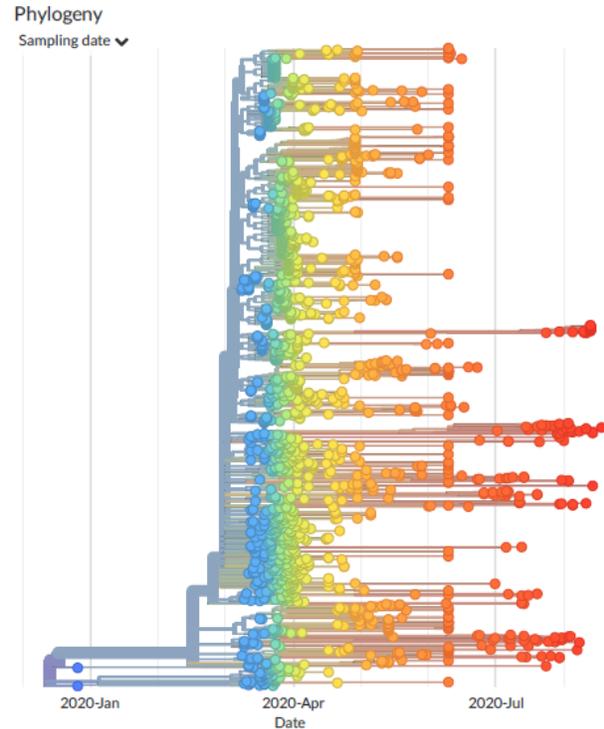
Explore the narrative by scrolling on the left panel, or click "explore the data yourself" in the top right to interact with the data.

Genomic Epidemiology SARS-CoV-2 in Michigan : MMWR week 37

Author: Heather Blankenship PhD¹

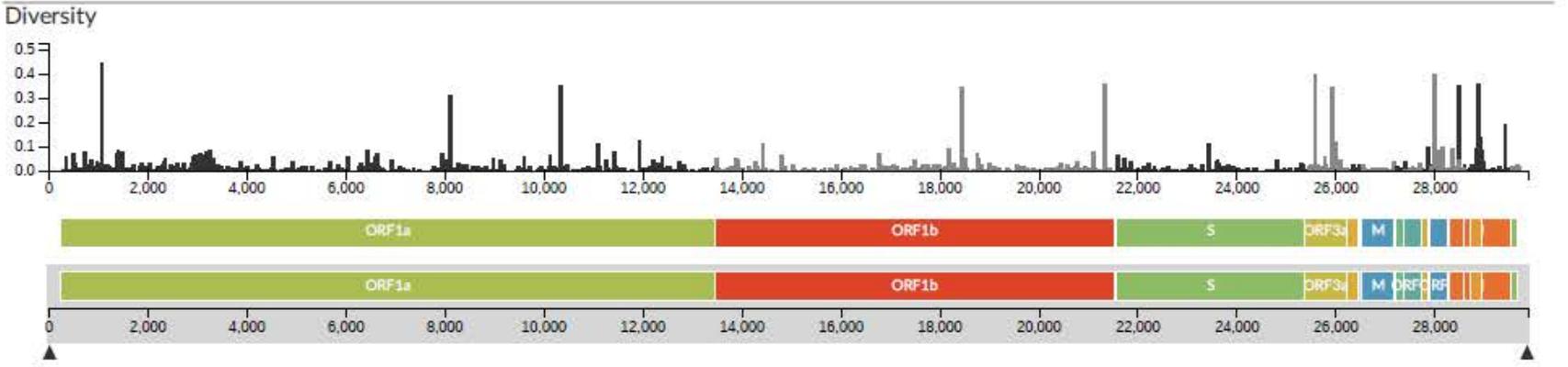
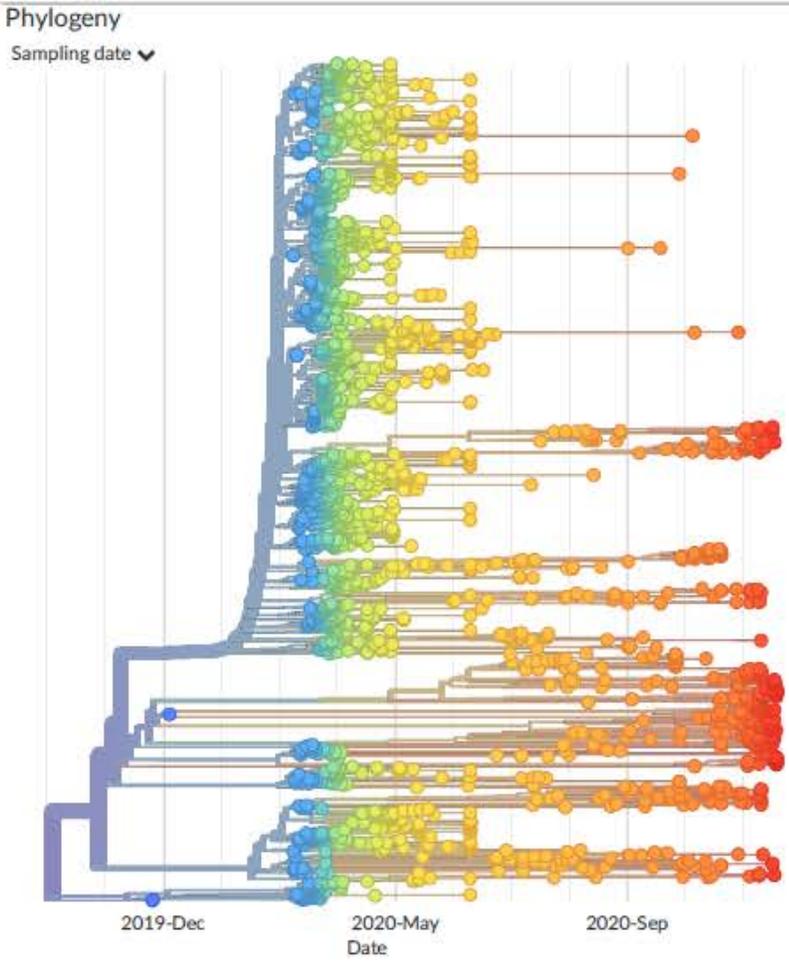
¹ Michigan Department of Health and Human Services, Bureau of Laboratory, Division Infectious Disease, Lansing, MI
Created: September 16, 2020

Updated: September 16, 2020



Summary

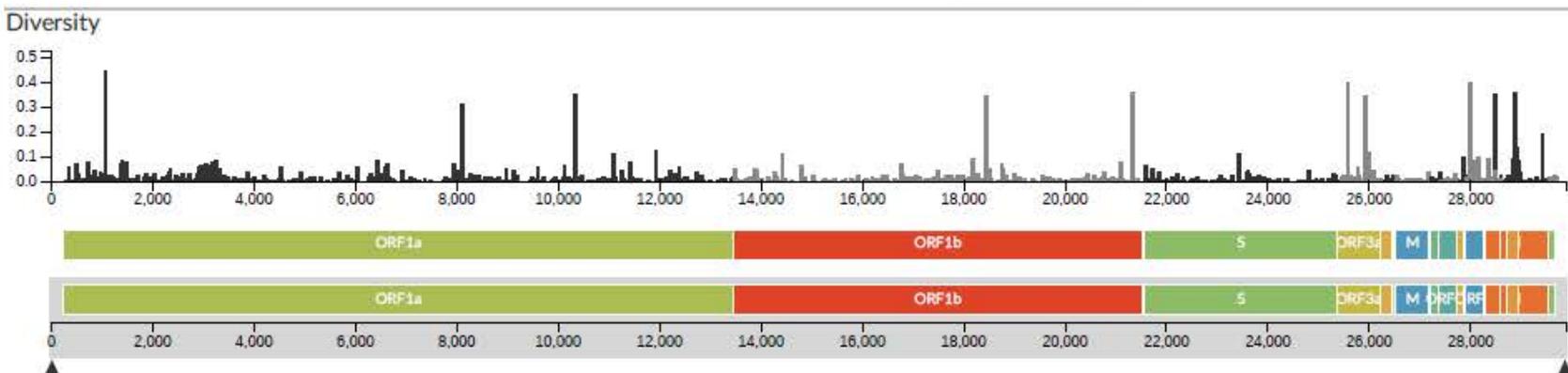
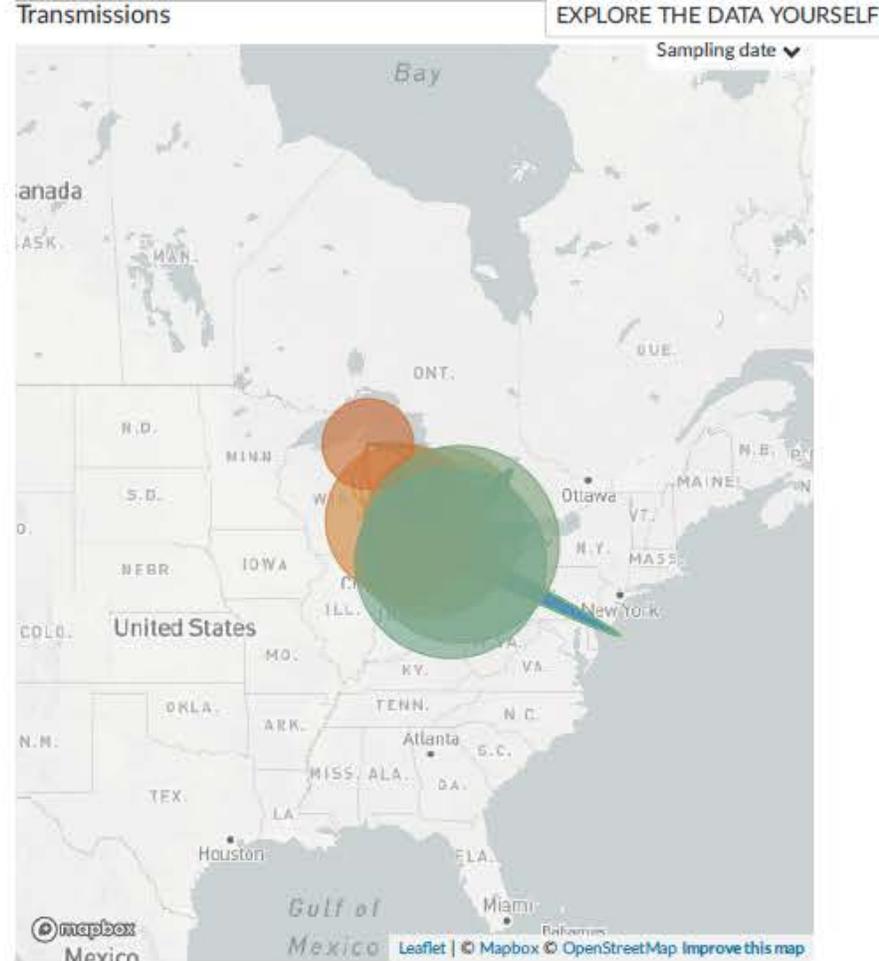
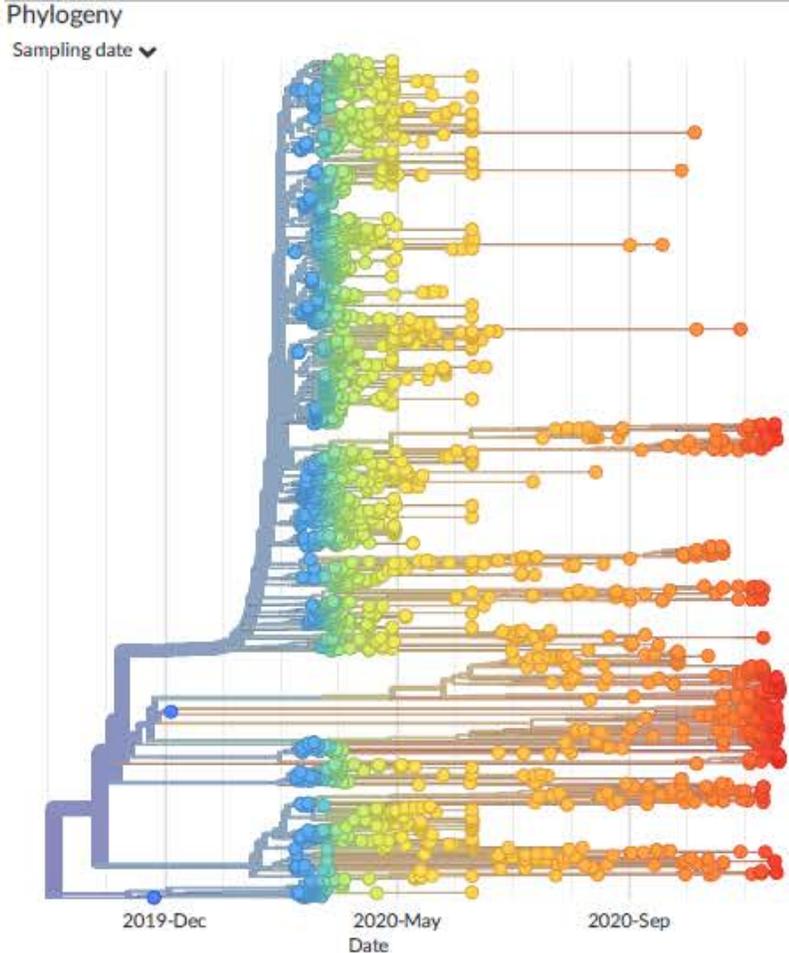
We have currently sequenced 2528 SARS-CoV-2 genomes since the first case was detected in Michigan. The first few pages will include the background information of SARS-CoV-2 sequencing. Updates and new genomic information is presented starting on page 6.



SARS-CoV-2 Sequencing Purpose

The purpose of analyzing the viral genomes are to:

- To understand the viral biology to help inform future scientific paths (potential vaccine development, identify environmental host and source of the virus, and general viral dynamics).
- To monitor for clinically important variants (assess association of clinical outcomes with different strain variants or identify variants that may disrupt diagnostic test targets).
- To inform public health action for future “flare-up” or potential seasonality (transmission networks).
- To establish national and regional baselines to assess the effectiveness of response strategies.
- To examine local and national transmission dynamics of the virus for immediate public health tracking in site specific areas.





Basic SARS-CoV-2 Overview

SARS-CoV-2

SARS-CoV-2 is classified as a coronavirus and the etiological agent responsible for COVID-19 infections. Coronaviruses are not a novel family of viruses and includes other known viruses such as, MERS and SARS, in addition to the common cold viruses that circulate each year. The nucleic acid material for these viruses are RNA encoded (instead of DNA).

In order for viruses to continue to spread and replicate, they have to infect human cells so that they can utilize the enzymes and machinery of the host cell for replication. The machinery (RNA polymerase) that is responsible for copying the RNA is error prone and lacks the ability to proofread and edit the mistakes. This step can lead to the accumulation of mutations in the viral genomes.

Not all mutations that are generated will be beneficial for the virus. Three events can occur from a mutation that is generated:

- the mutation causes the virus to no longer be viable - these viruses will most likely never be isolated
- the mutation has no effect on the virus - these viruses may be isolated from multiple people, redundancy in the genetic code allows for mutations to occur and not impact the protein structure or activity
- the mutation will allow the virus to spread among the population and may result in a virus that is more pathogenic

For some of the mutations that occur, we are still unsure of the associations between these mutations and clinical outcomes or presentation of symptoms. We are also unable to identify whether a specific mutation will result in a more pathogenic strain or change the disease severity without performing the additional molecular epi analysis using a complete study population, even then, we will face limitations that may impact the associations that we see with various mutations and outcomes.

Demographics

Discrepancies may be seen for the total metadata and genomic sequences, due to sequences that pass QC but are lower quality being filtered out of the phylogenetic analysis or duplications of samples.

Gender

total (n=2528)	gender
1186	female
1314	male
26	unknown

Age

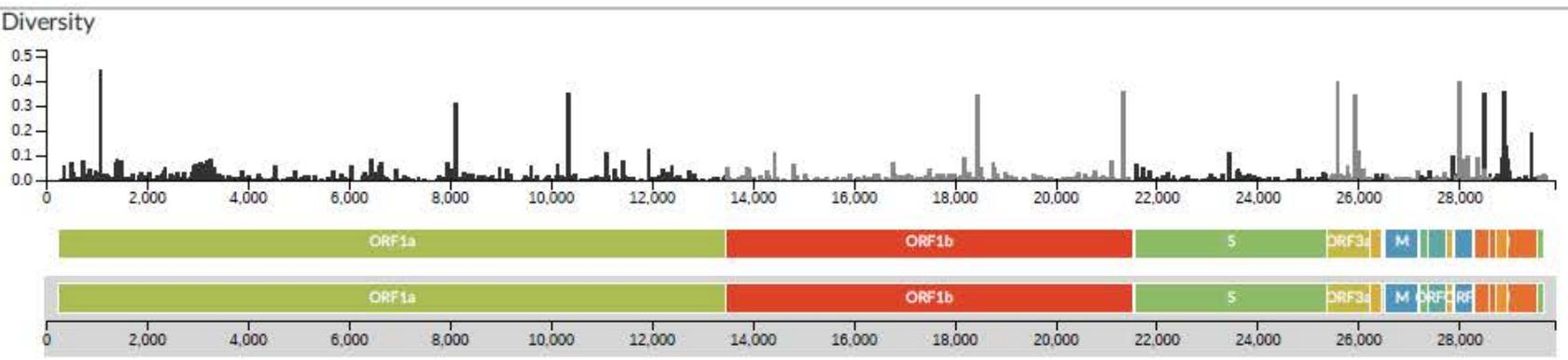
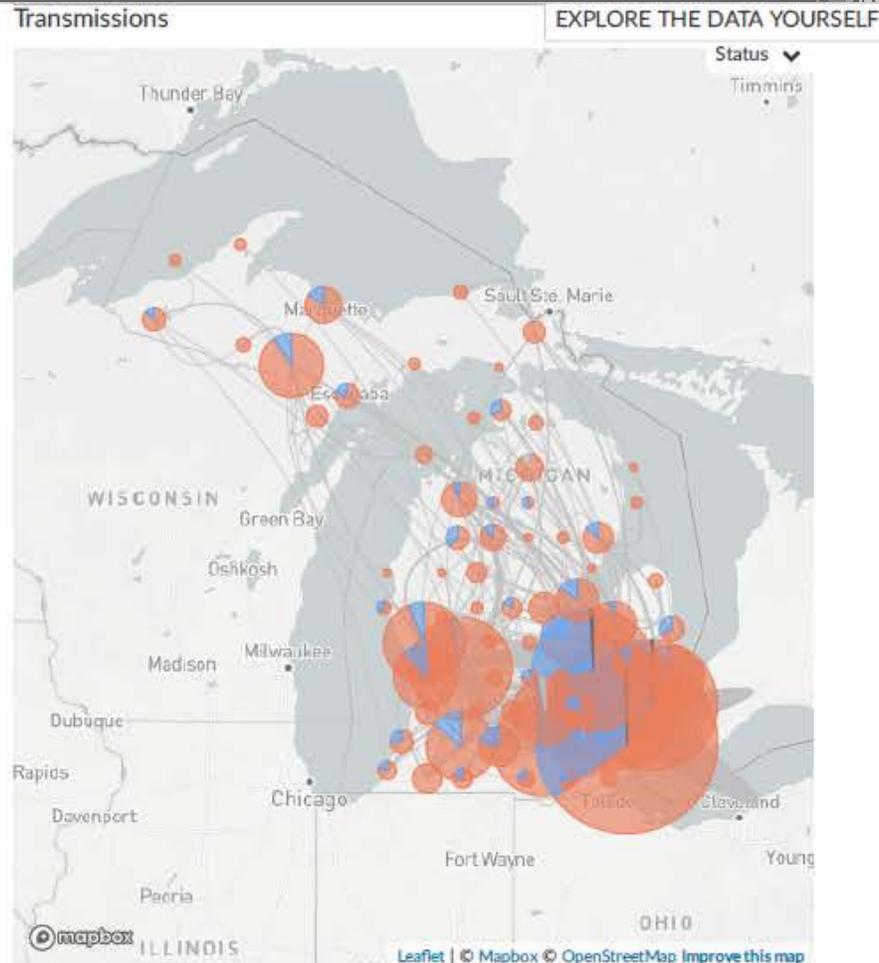
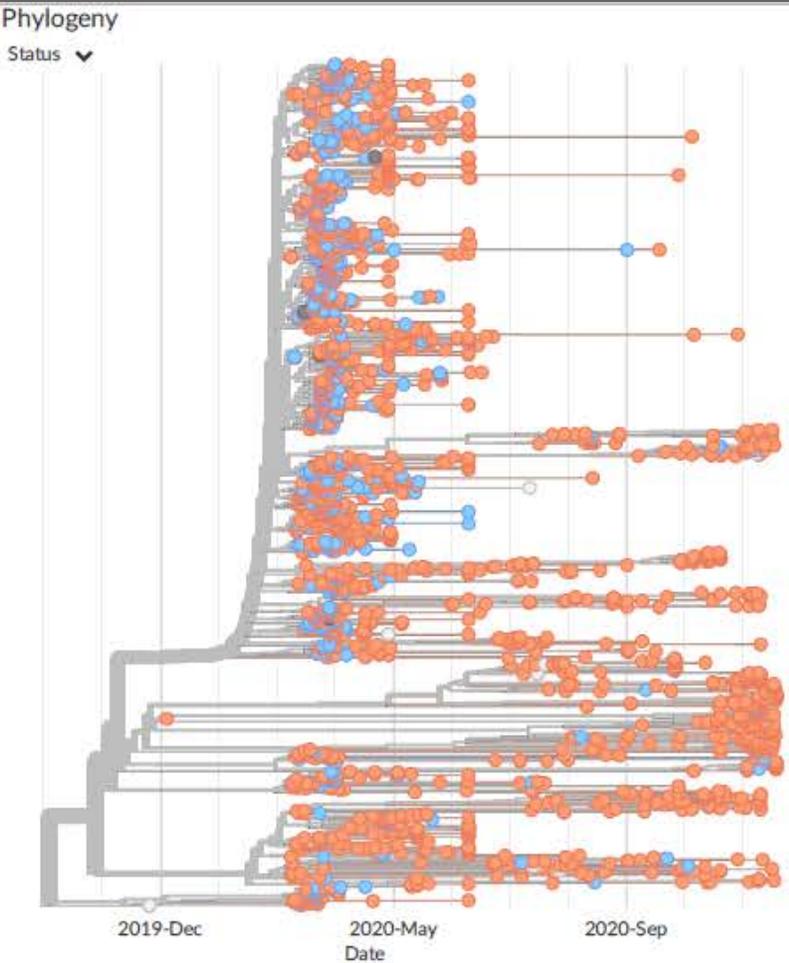
total (n=2528)	age
75	0-18 years
1499	19-65 years
950	>66 years
4	unknown

Regional Distribution

total (n=2224)	region
254	Region 1
593	Region 2N
555	Region 2S
389	Region 3
150	Region 5
349	Region 6
68	Region 7
126	Region 8

Status of Individual

Overlaying the patient status on the phylogenetic tree gives no indication of a specific clade or cluster associated with deceased patients.



- Questions?

SARS-CoV-2 Variants Update

Vivien Dugan

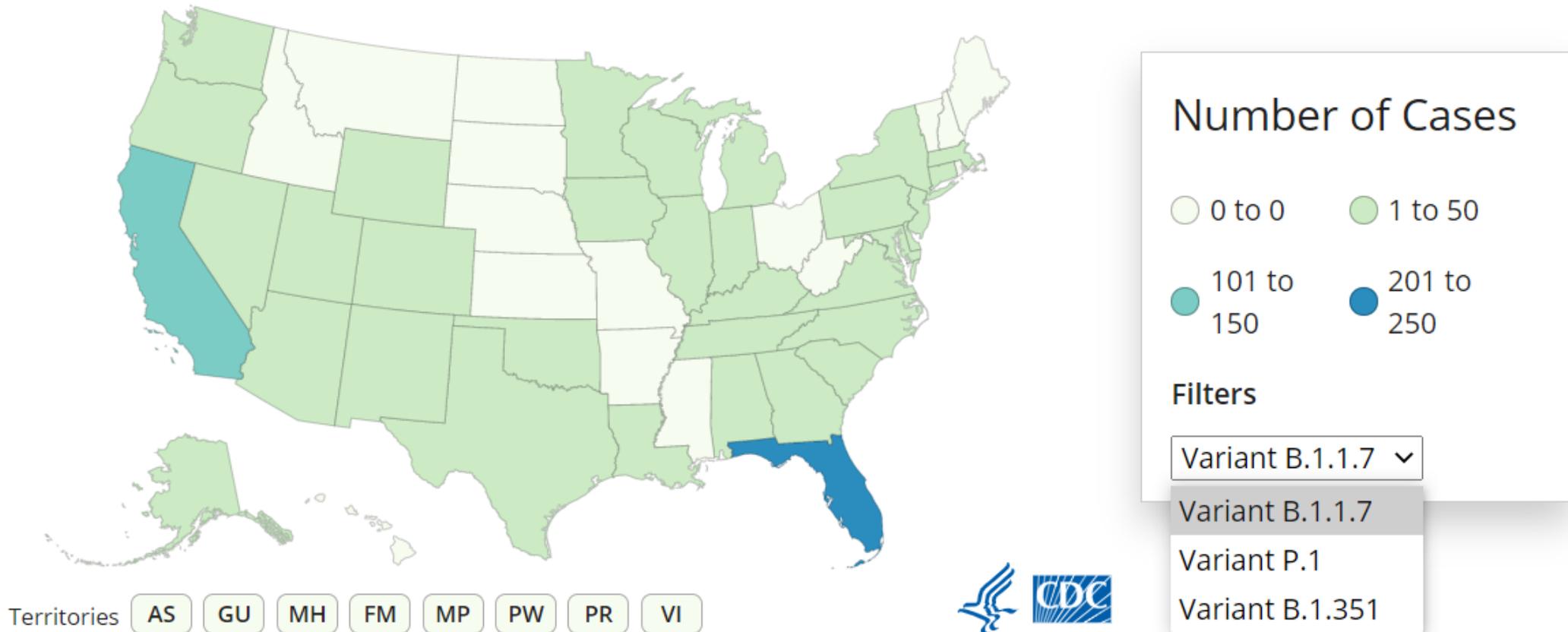
CDC Laboratory and Testing Task Force
for the COVID-19 Response



U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

US COVID-19 Cases Caused by Variants

<https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant-cases.html>





Vaccine Breakthrough Case Investigations

Information for Clinical Labs

Feb 8, 2021

Leisha Nolen, MD PhD

Goal

- Investigate SARS-CoV-2 infection among people who received COVID-19 vaccine in order to identify trends or clustering in patient characteristics, the administered vaccine, or the infecting virus
 - High risk groups or conditions
 - Waning immunity
 - Vaccine compromise
 - inadequate cold-chain, issues during shipping, storage, or administration
 - Viral mutations or variants

Vaccine breakthrough case definition

- U.S. resident who has **SARS-CoV-2 RNA or antigen positive** respiratory specimen collected **≥14 days after completing** the primary series of an **FDA-authorized SARS-CoV-2 vaccine**
- Exclusions
 - Received vaccine not authorized or approved by FDA
 - Did not receive full primary series
 - Positive specimen collected <14 days after completing primary series
 - **Previous positive COVID test <45 days prior to current positive test**

Investigation

- Reported through the State Health Departments
- Collect:
 - Epidemiologic data
 - Demographics
 - Basic risk factors
 - Vaccine details
 - COVID-19 infection details
 - Laboratory data
 - Viral characterization
 - Immune characterization (rarely)

Viral Characterization

- Evaluating changes in the SARS-CoV-2 Virus
 - Genomic Sequence
 - Sequence is already performed locally
 - Performed on material sent by local lab
 - Viral isolate
 - RNA
 - Respiratory specimen
 - Changes in the virus that allow it to evade neutralization by convalescent/vaccinated serum
 - Would require viable viral sample

Sample for viral testing

- The original test sample
 - Respiratory specimen
 - Isolated RNA or virus
- Sample storage and shipment
 - 1.0–2.0 mL screw cap microcentrifuge tubes with an O-ring
 - Labeled with the de-identified REDCap survey ID
 - State health department should provide this number
 - Store at –70C until shipment
 - CDC will provide specific paperwork for shipment

Immune Characterization

- Determine if breakthrough cases have decreased immune response to vaccine
 - Ideally, serum taken between vaccine and infection
 - Realistically, serum taken as soon as possible after acute infection
- Retrieve **existing serum** that was from between vaccination and SARS-CoV-2 infection, or serum taken in the first 7 days of infection
 - Expect we will rarely have access to these samples

Clinical Labs Roles

- Identifying samples from breakthrough cases
 - Working with health departments
 - Some sites are adding vaccine questions to their requisition forms
- Holding samples from breakthrough cases
- Transfer samples for testing
 - Some states are doing local viral sequencing
 - Shipping to CDC directly or through PHL
 - Forms are similar to the NS3, but specific for this project

COVID-19 vaccine breakthrough case investigation team

Email Contact: eocevent531@cdc.gov

For more information, contact CDC Emergency Operations Center
770-488-7100
www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



FDA Update

Tim Stenzel

U.S. Food and Drug Administration (FDA)



U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

U.S. Food and Drug Administration (FDA)

- **COVID-19 Emergency Use Authorization (EUA) Information for Medical Devices**

<https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations>

- **COVID-19 In Vitro Diagnostic EUAs**

<https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas>

- **COVID-19 Frequently Asked Questions**

<https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/coronavirus-disease-2019-covid-19-frequently-asked-questions>

- **COVID-19 Updates**

<https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#2019-ncov>

- **FDA Townhall Meetings**

<https://www.fda.gov/medical-devices/workshops-conferences-medical-devices/virtual-town-hall-series-immediately-effect-guidance-coronavirus-covid-19-diagnostic-tests-06032020>

- **Independent Evaluations of COVID-19 Serological Tests**

<https://open.fda.gov/apis/device/covid19serology/>

U.S. Food and Drug Administration (FDA)

- **COVID-19 Diagnostic Development**

CDRH-EUA-Templates@fda.hhs.gov

- **Spot Shortages of Testing Supplies: 24-Hour Support Available**

1. Call 1-888-INFO-FDA (1-888-463-6332)

2. Then press star (*)

- **FDA MedWatch**

<https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program>

CDC Social Media



<https://www.facebook.com/CDC>

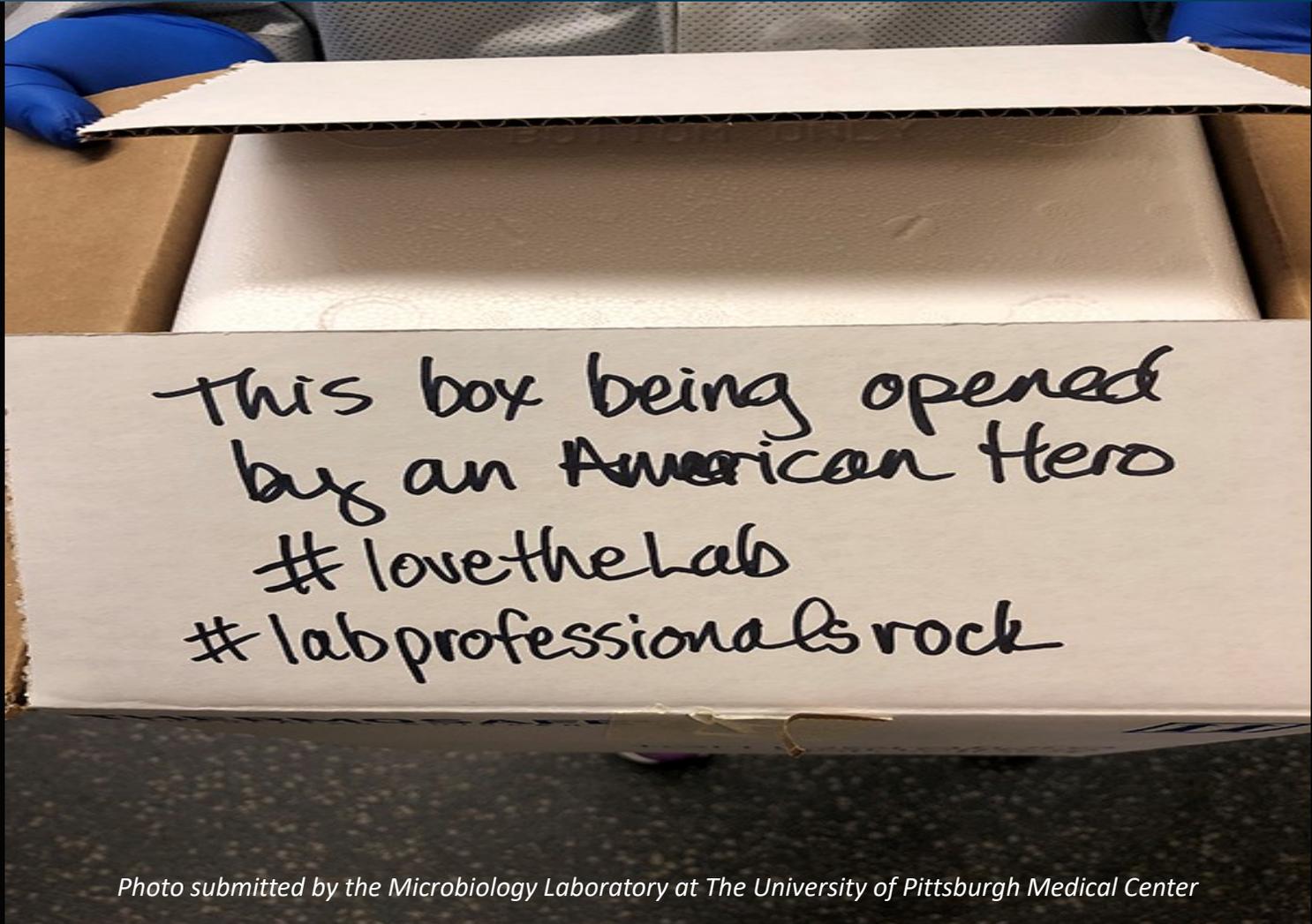


<https://twitter.com/cdcgov>



<https://www.linkedin.com/company/cdc>

Thank You For Your Time!



This box being opened
by an American Hero
#lovethelab
#labprofessionalsrock

Photo submitted by the Microbiology Laboratory at The University of Pittsburgh Medical Center