Detecting and prioritizing SARS-CoV-2 variants

COVID-19 Genomic Epidemiology Toolkit: Module 2.6: Detecting & prioritizing variants

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cdc.gov/coronavirus
Part 1: Introduction
1.1 What is genomic epidemiology?
1.2 The SARS-CoV-2 genome
1.3 How to read phylogenetic trees
1.4 Emerging variants of SARS-CoV-2

Part 2: Case Studies
2.1 SARS-CoV-2 sequencing in Arizona
2.2 Healthcare cluster transmission
2.3 Community transmission
2.4 Superspreading event
2.5 Confirming reinfection
2.6 Detecting & prioritizing variants
2.7 Wastewater-based variant tracking

Part 3: Implementation
3.1 Getting started with Nextstrain
3.2 Getting started with MicrobeTrace
3.3 Phylogenetics with USher
3.4 Walking through Nextstrain trees
3.5 Public data repositories
3.6 Sequencing strategies
CDPHE sequencing capacity

- Funded PulseNet Regional Lab
  www.cdc.gov/pulsenet/index.html

- State support for COVID-19 specific positions and additional instrumentation

- CDC/State funded cloud computing resources for genome sequence analyses
CDPHE sequencing priorities: August – December 2020

- First run completed in August 2020
- > 450 sequences supporting more than 100 individual investigations

https://nextstrain.org/groups/spheres/ncov/colorado?c=clade_membership&dmax=2020-12-31&dmin=2020-08-01&f_division=Colorado&p=full
CDPHE sequencing priorities: August – December 2020

- Initial focus on congregate living facilities for:

  1. Outbreak investigation
     - Was virus introduced into a facility by one transmission event or many?
  2. Confirming reinfection
     - Was a particular resident reinfected, or was the viral shedding from a previous infection?

- This information informed cohorting and contact tracing in subsequent outbreaks at similar facilities.
Emergence of VOC B.1.1.7

- First described in December 2020
- Classified as Variant of Concern (VOC)
- Deletion within spike (S) gene
- Produces a characteristic S Gene Target Failure (SGTF) on the ThermoFisher TaqPath RT-PCR assay.

- Module 1.4 – Emerging variants of SARS-CoV-2

CDPHE sequencing priorities: Dec 2020 – present

- **Pivot priority to SGTF**
  - SGTF specimens identified at clinical and commercial labs routed to CDPHE
  - First U.S. case of B.1.1.7 detected in Colorado, Dec 2020
  - Unlike other locations, 100% of SGTF specimens sequenced in CO from Dec 2020 - Jan 2021 were B.1.1.7

[B.1.1.7 as % of sequenced SGTF US Data, Illumina-Helix](www.helix.com/pages/helix-covid-19-surveillance-dashboard)
Variant detection and response prioritization

Variant emergence increased statewide engagement for a broad surveillance program

- Case investigation and contract tracing (CI/CT):
  - Daily meetings
  - Communicate sequence data as needed

- Epidemiology feedback:
  - Helps with contact tracing
  - Consistently detects secondary positive cases
  - Limited by turnaround time
Example B.1.1.7 cluster investigation

- Individual specimen with SGTF identified at a commercial laboratory
- Index specimen unavailable for sequencing
- But CI/CT identified 10 additional B.1.1.7 cases among family and coworkers
Example B.1.1.7 cluster investigation

Conserved spike gene mutations
Detecting other variants with sentinel surveillance

- Surveillance by convenience sampling
  - **Random sampling:** 30 positive specimens per week from each clinical laboratory within statewide sentinel surveillance network
  - **CDPHE-tested:** all positive specimens identified at the state lab

- Better surveillance sampling $\rightarrow$ sequencing increased $>5$-fold:
  - December 2020: 180 specimens / week
  - April 2021: 1,000 – 1,200 specimens / week
Detecting other variants with sentinel surveillance

- Surveillance sequencing led to the detection of the first B.1.351 in Colorado
  - Multiple positives were identified as B.1.351 from the same county and connected to a congregate living facility (March 1, 2021)
  - Case investigation and contact tracing at the facility identified additional cases of B.1.351
  - The following week (March 8, 2021), multiple specimens from another county were identified among members of a single family
Two B.1.351 clusters identified in March 2021

Cluster 1 (Facility) Weeks 1-2

Cluster 2 (Family) Week 2

Unrelated B.1.351

Community case with no known connection to the facility

Mutations

26 30 34 38
CO continues to track VOC/VOI (Variant of Interest) proportions

Excludes all:
- Known SGTF submissions
- Known VOC/VOI investigations
- Special studies with CDC

CDC COVID Data Tracker:
https://covid.cdc.gov/covid-data-tracker/#variant-proportions
Sequencing supports understanding virus transmission and COVID-19 severity

- VOC B.1.427/B.1.429
- MMWR
- Vaccine breakthrough
- Reinfection
- Wastewater surveillance
  - See Module 2.7

www.cdc.gov/mmwr/volumes/70/wr/mm7019e2.htm
Summary

- Sequencing efforts support both national and statewide characterization of SARS-CoV2 transmission and COVID-19 severity.
- Sequencing adds valuable information for case investigation, contact tracing, and outbreak response
  - Most VOC cases identified by sequencing have led to detection and quarantine of secondary positives.
- Contribution of SGTF investigation to overall surveillance in CO
  - Layered approach to balance investigation of all SGTFs
  - Continue to monitor whether targeted surveillance impacts overall surveillance
- Detecting emerging variants
  - Unbiased, statewide surveillance is necessary to monitor and detect emerging VOCs not associated with SGTFs.
Learn more

- Other modules
  - Emerging variants of SARS-CoV-2 – Module 1.4
  - Distinguishing workplace from community transmission – Module 2.3

- COVID-19 Genomic Epidemiology Toolkit
  - Find further reading
  - Subscribe to receive updates on new modules as they are released
  - go.usa.gov/xAbMw
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