Confirming SARS-CoV-2 reinfection with whole genome sequencing

COVID-19 Genomic Epidemiology Toolkit: Module 2.5

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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

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 genome repositories
3.6 Sequencing strategies
COVID-19 reinfection cases

- Reinfection cases have been reported, but they are rare:
  - Risk was estimated at 0.02%, and the reinfection incidence rate was 0.36 per 10,000 person-weeks (Abu-Raddad et al. 2020)

- CDC protocol for investigating suspected SARS-CoV-2 reinfection:
  - Persons with or without COVID-19-like symptoms ≥90 days after initial infection/illness
  - Persons with COVID-19-like symptoms 45-89 days after initial infection/illness
  - Sequencing of paired respiratory specimens (one from each infection episode) is recommended for confirmation

Abu-Raddad et al. (2020) Assessment of the risk of SARS-CoV-2 reinfection in an intense re-exposure setting, PMID: [33315061](#)

Reinfection case overview

32-year-old-person experiencing homelessness

- June 2020 - Shelter A
  - Tested in response to on-site staff with positive test
  - Symptoms: fever, sore throat, cough, headache
  - Recovered, no hospitalization required

- October 2020 - Shelter B
  - Tested in response to resident with positive test
  - Symptoms: general cold symptoms, reported feeling very ill
  - Recovered, no hospitalization required
Phylogenetic tree of case specimens

Specimens taken 138 days apart

June 2020 Specimen

October 2020 Specimen
## Genotypic characterization of sequences

<table>
<thead>
<tr>
<th>Nextclade Designation</th>
<th>June 2020</th>
<th>October 2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pangolin Lineage</td>
<td>B.1 (Version 2021-04-14)</td>
<td>B.1.2 (Version 2021-04-14)</td>
</tr>
<tr>
<td>GISAID ID</td>
<td>EPI_ISL_672360</td>
<td>EPI_ISL_672367</td>
</tr>
</tbody>
</table>
| Amino Acid Substitutions | **Spike:** D614G, T1231A  
N: S194L  
NS3: A110S  
**NSP12:** P323L  
NSP13: G203C, P82T | **Spike:** D614G, K1191N  
M: D209Y  
N: P67S, P199L  
NS3: G172V, Q57H  
NS7a: A8T  
NS8: S24L  
NSP2: T85I  
NSP3: E1801K, M102I  
NSP5: L89F  
**NSP12:** P323L  
NSP14: N129D  
NSP16: R216C |
Confirming reinfection findings

- The patient was part of separate, larger outbreaks
  - Outbreak in Shelter A, June 2020
    - Exposure dates May 22 – July 7, 2020
    - Included 19 residents and 7 staff
    - WGS performed on 4 specimens
  - Outbreak in Shelter B, October 2020
    - Exposure dates October 15 – November 2, 2020
    - Included 14 residents and 1 staff
    - WGS performed on 9 specimens
Outbreak in Shelter A, June 2020

Specimens (n=4) collected
May 22 – June 3, 2020

June 3, 2020 specimen
Outbreak in Shelter B, October 2020

Specimens (n=9) collected October 15 – 23, 2020

10/19/2020 specimen

Mutations
Summary

- Reinfections seem to be rare, but previous SARS-CoV-2 infection may not confer immunity against a different variant.

- WGS of paired specimens can confirm reinfection of SARS-CoV-2:
  - Case study specimens from June 2020 and October 2020 exhibited
    1. Distinct clade and lineage assignments
    2. Specific mutation patterns
  - Alternative: similar sequences would suggest persistent infection.

- Additional epi data can inform the genomic epidemiologic investigation:
  - Both positive tests reported during outbreaks more than 3 months apart at separate facilities.
Learn more

- Other introduction modules
  - Community Transmission – Module 2.3
  - Superspreading Event– Module 2.4

- COVID-19 Genomic Epidemiology Toolkit
  - Find further reading
  - Complete a feedback survey
  - Subscribe to receive updates on new modules as they are released
    go.usa.gov/xAbMw
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.
Further Reading:


Resources: