SYNOPSIS
03/11/2020

Review of “Genomic diversity of SARS-CoV-2 in coronavirus disease 2019 patients”


One-Minute Summary

- Metatranscriptome sequencing (direct sequencing of transcripts) of bronchoalveolar lavage fluid (BALF) was used to investigate the **intra-host diversity of SARS-CoV-2**, the causative agent of COVID-19 and to examine the **microbiota in COVID-19 patients**.
- Between December 18–29, 2019, BALF from COVID-19 patients (N=8) in Wuhan were collected (ranging from four to 15 days after symptom onset):
  - The patients were between **40 and 61 years old** and five were male.
  - Six patients were admitted to intensive care.
  - Five patients died, two recovered and the outcome for one patient was unknown.

**Intra-host variants in COVID-19 patients:**
- **84 intra-host variants** were identified. 2/84 variants were found in more than one patient, one of which was found in all seven patients (one BALF was excluded from the analysis because of low genome coverage).
- The **median number of intra-host variants was one to four (range 0-51)**. The number of variants did not correlate with days after symptom onset or age of the patient.
- The authors **did not find evidence of transmission of intra-host variants**.
- It is not clear whether intra-host variants occurred before transmission (infection by multiple strains) or after transmission (within host strain evolution); however, the high number of variants observed in some patients suggests that COVID-19 may evolve **in vivo** post-infection.

**Microbiota in COVID-19 patients:**
- The microbiota of the eight COVID-19 BALF was compared to BALF from 25 patients with virus-like community-acquired pneumonia (CAP) and 20 healthy individuals.
- Six COVID-19 specimens clustered with the pathogen-enriched microbiota type and two clustered with the commensal-enriched microbiota type. **No distinct microbial pattern** was observed.
- Overall, the **microbiota in COVID-19 patients were similar to the dysbiosis (i.e., imbalances in the microbial communities) seen in patients with CAP.**
Additional Information

Intra-host variants in COVID-19 patients:
- Variants were found in all COVID-19 genes except for the E (envelope) gene and ORF10 gene. This distribution is similar to the distribution of polymorphisms seen in the COVID-19 population of 110 strains.
- Only 3/84 intra-host variants were found in the COVID-19 strain population. Further, analysis of two patients believed to be part of a person-to-person transmission event showed that intra-host variants found in the index case was not found in the secondary case. This suggests that transmission of intra-host variants does not occur; however, the data are limited.
- Correlation of the number of intra-host variants with severity or outcome was not determined.

Microbiota:
- The CAP specimens were collected from four hospitals in China between 2014 and 2018. Age range for CAP patients was 22-85 years; severity and outcomes were not reported. Demographic information and recruitment criteria for healthy patients were not provided.
- The absolute microbial load in the COVID-19 and other specimens is unknown.
- Overall, microbial diversity in the COVID-19 and CAP specimens was significantly lower compared to the healthy controls. The authors suggest that this could be due to the use of antibiotics in treating patients with pneumonia; however, prescribing data was unknown.

PHO Reviewer’s Comments
- Metatranscriptome sequencing is performed directly from specimen and cannot differentiate between colonization and infection. For detection of RNA viruses, like COVID-19, the method cannot distinguish between live and dead virus.

Citation


Disclaimer

This document was developed by Public Health Ontario (PHO). PHO provides scientific and technical advice to Ontario’s government, public health organizations and health care providers. PHO’s work is guided by the current best available evidence at the time of publication.

The application and use of this document is the responsibility of the user. PHO assumes no liability resulting from any such application or use.

This document may be reproduced without permission for non-commercial purposes only and provided that appropriate credit is given to PHO. No changes and/or modifications may be made to this document without express written permission from PHO.
Public Health Ontario

Public Health Ontario is a Crown corporation dedicated to protecting and promoting the health of all Ontarians and reducing inequities in health. Public Health Ontario links public health practitioners, frontline health workers and researchers to the best scientific intelligence and knowledge from around the world.

For more information about PHO, visit publichealthontario.ca.