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SYNOPSIS

03/11/2020

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

Article citation: Shen Z, Xiao Y, Kang L, Ma W, Shi L, Zhang L, et al. Genomic diversity of SARS-CoV-2 in coronavirus disease 2019 patients. Clin Infect Dis. 2020 Mar 4 [Epub ahead of print]. Available from: https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa203/5780800

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

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Review of "Genomic diversity of SARS-CoV-2 in coronavirus disease 2019 patients". Toronto, ON: Queen's Printer for Ontario; 2020.

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