CanCOGeN RCanGeCO

Canadian National COVID Genomics Surveillance for Emerging Variants of Concern and other Priorities

2020-12-23

The Canadian COVID-19 Genomics Network (CanCOGeN) is performing genomic surveillance of circulating SARS-CoV-2 in Canada to track its spread, monitor for variants of concern (VOCs) that might impact transmissibility or disease severity, assist in outbreak investigations, and assess the impact of public health interventions. Recent reports of emerging VOCs with enhanced transmissibility have been reported in the UK and South Africa. The potential for rapid spread of these variants affirms the need for ongoing and enhanced genomic surveillance in Canada and worldwide. Here we set out the national priorities for genomic surveillance, including targeted surveillance of these emerging VOCs.

1) **Targeted Surveillance**

   a) **Priority VOCs**

      i) **UK and SA VOCs.** The UK VOC (VOC-202012/01) was first detected in October 2020 in the United Kingdom. It is correlated with increased transmissibility in the UK and has been reported in other countries. A South African VOC, currently designated 501Y.V2, similarly correlates with increased transmissibility in South Africa. Both variants are characterized by an "N501Y" mutation in the SARS-CoV-2 spike protein's receptor-binding domain. CanCOGeN has identified both VOCs as priorities for retrospective and prospective targeted surveillance.

         (1) Retrospective targeted surveillance

            (a) All international travellers, including the United States, and close contacts, from September 1, 2020, to the present.

         (2) Prospective targeted surveillance

            (a) All international travellers, including the United States, and close contacts, from the present until further notice.

   b) **Multi-target COVID-19 RT-PCR tests with target dropouts.** COVID-19 diagnostic tests with multiple gene targets that fail to detect one or more targets indicate a risk for testing efficacy. The UK VOC-202012/01 notably can test negative for the S-gene target but positive for other targets using the three-target assay (N, ORF1ab, S) from Thermo Fisher (TaqPath).

   c) **Reinfection.** We define reinfection as clinical recurrence of symptoms compatible with COVID-19, accompanied by positive PCR (Ct<35), more than 90 days after the onset of the primary infection, supported by close contact exposure or outbreak settings, and no evidence of another cause of infection[1]. Reinfection indicates possible infection by immune-escape variants.

[1] Yahav, D. *et al.* Definitions for COVID-19 reinfection, relapse and PCR re-positivity. *Clin. Microbiol. Infect.* (2020) doi:10.1016/j.cmi.2020.11.028

d) **Severe acute COVID-19 in individuals <50 years old without significant comorbidities.** Disproportionately severe disease in individuals who are otherwise healthy may indicate a change in pathogen virulence resulting in a more florid clinical phenotype, and is thus relevant for surveillance and potentially for patient management.

e) **Vaccinated individuals with subsequent laboratory-confirmed SARS-CoV-2 infection.** Although there is a limited number of vaccinated individuals at this time, that number is expected to grow. It is anticipated that with the roll-out of vaccines there will be a need to monitor for and characterize potential vaccine escape variants.This likely would require simultaneous monitoring for immune correlates of vaccine response, assessment of seroprotection, and systematic genomic testing of post-vaccine infections to monitor for vaccine-escape mutants.

f) **Known or suspected superspreading events.** Given the proposed potential for increased transmissibility of the UK and SA VOCs, and the N501Y mutant, sequencing multiple samples from a known or suspected superspreading event may identify such mutations.

DEFINITION: A superspreading event is a type of outbreak where there is additional epidemiological and/or genomic evidence of one person with overdispersed* transmission of COVID-19, (*i.e.*, directly transmitting to at least five non-household individuals).

EXCLUSIONS: This definition excludes large or propagated outbreaks with no evidence of overdispersion.

*The statistical concept of overdispersion refers to the few individuals disproportionately and directly infecting a large number of secondary cases relative to the "average" infectious individual, whose infectiousness may be represented by R_0, which is estimated at 2.0 for COVID-19[2].

Specimens identified from these targeted populations should be forwarded to CanCOGeN partner labs for priority genome sequencing and analysis.

2) **Continued random sampling for routine national genomic surveillance.** CanCOGeN sampling guidelines for national priorities include random sampling for routine SARS-CoV-2 genomic surveillance. Routine surveillance is used to monitor existing variants of concern, identify emerging variants of concern, track viral transmission, and assess the effectiveness of public health interventions. Random sampling for routine genomic surveillance is ongoing and will continue.

3) **Continued sampling to investigate SARS-CoV-2 outbreak clusters.** CanCOGeN sampling guidelines include strategies to investigate and respond to SARS-CoV-2 outbreak clusters. Sampling for outbreak investigations is ongoing and will continue.

[2] Liu, Y., Gayle, A. A., Wilder-Smith, A. & Rocklöv, J. The reproductive number of COVID-19 is higher compared to SARS coronavirus. *J. Travel Med.* **27**, (2020)