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# SARS-CoV-2 Genomics for Public Health Surveillance

Dr. Samir N. Patel, PhD FCCM (D) ABMM

Alex Marchand-Austin, MSc

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PHO Rounds

## Disclosures

- None of the presenters at this session have received financial support or in-kind support from a commercial sponsor.
- None of the presenters have potential conflicts of interest to declare

# Outline

- Role of whole genome sequencing in public health
- Whole genome sequencing of SARS-CoV-2
- SARS-CoV-2 genomics in Ontario
  - Testing algorithms and specimen flow
  - Reporting
- Genomics and outbreaks
- Future directions

# Objectives

Participants will learn about:

- Application of whole genome sequencing for supporting the pandemic response
- Describe the key steps in the process for whole genome sequencing of SARS-CoV-2 in Ontario
- Discuss the role of whole genome sequencing for supporting the pandemic response
- Describe the relationship between mutations and lineages for SARS-CoV-2 variants of concern/interest
- Locate and identify key components of PHO genomics program outputs to support surveillance efforts

# Acronyms

- WGS = whole genome sequencing
  - Laboratory method for determining the genetic sequence of the SARS-CoV-2 virus
- VOC/VOI = variant of concern/variant of interest
  - Genetic variant of SARS-CoV-2 with evidence of characteristics of clinical and/or public health significance
- PCR = polymerase chain reaction
  - Laboratory method used for detection of specific regions in the genome
- Ct = cycle threshold
  - Numerical value used in PCR analysis that is associated with the amount of target genetic material in the specimen. Higher = less, lower = more



# **Role of Whole Genome Sequencing in Public Health**

# Whole Genome Sequencing in Microbiology

- The last two decades have seen significant growth in WGS of pathogens
- 2002- 2003:
  - SARS-CoV: only 3 genomes publicly available in 1<sup>st</sup> month; 31 genomes in 3 months
- 2019-2021:
  - SARS-CoV-2: 6 genomes within 3 weeks; 60,000 within 6 months
  - As of Aug 19, 2021: 2,892,198 genomes are publicly available.
- Improvement in technology, cost and throughput

World Health Organization, Genomic sequencing of SARS-CoV-2: a guide to implementation for maximum impact on public health, 2021



# Application of WGS in Microbiology

- Development of diagnostic assays
- Understanding pathogen virulence
- Detection and characterization of antimicrobial resistant genes
- Monitoring changes in the pathogen (genomic epidemiology)
- Vaccine development/breakthrough
- Assessing re-infection
- Outbreak investigation/support

World Health Organization, Genomic sequencing of SARS-CoV-2: a guide to implementation for maximum impact on public health, 2021

# Impact of Genomics in Public Health

- 2009 pH1N1: assessment of reproduction number based on gene sequences; retrospective testing identified cases 2 months prior to 1<sup>st</sup> case was sampled
- 2012 MERS: identified camels as reservoir of MERS and showed multiple independent transmission events from camels to humans
- 2013-2016 Ebola: real-time analysis assisted in understanding of the origin, transmission, and evolution of the virus; spread was mainly by human to human transmission
- 2016 Zika: infection associated with fetal microcephaly and other developmental abnormalities; phylogenetic studies showed introduction of a genotype circulating in Asia a year prior to the disease detection

World Health Organization, Genomic sequencing of SARS-CoV-2: a guide to implementation for maximum impact on public health, 2021



# Whole Genome Sequencing of SARS-CoV-2

## Overview

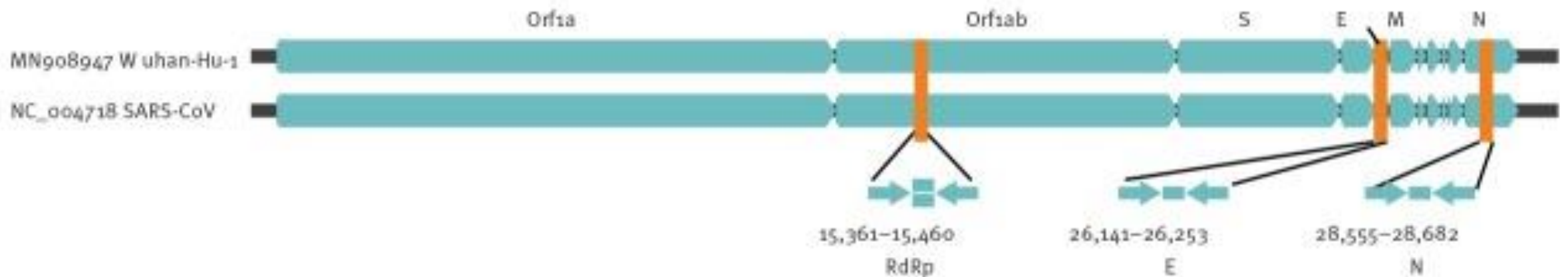
## SARS-CoV-2

- The SARS-CoV-2 virus has an RNA genome made up of roughly 30,000 bases
- The genome codes for 6 main proteins that perform functions for replication, infection, and virus structure
- The spike (S) protein is responsible for binding to specific receptors on human cells that allow the virus to enter and start replicating
- As the virus replicates, errors are introduced that can lead to changes in the genome sequence and function of proteins

Lu R, et al, 2020; Hu B, et al, 2020

## WGS in developing SARS-CoV-2 diagnostic assays

- Dec 31, 2019: WHO China office informed of cases of pneumonia with unknown etiology
- Jan 10, 2020: 1<sup>st</sup> genome was publicly posted
- Jan 12, 2020: 4 additional genomes were posted
- Facilitated the development of a diagnostic test specific to SARS-CoV-2



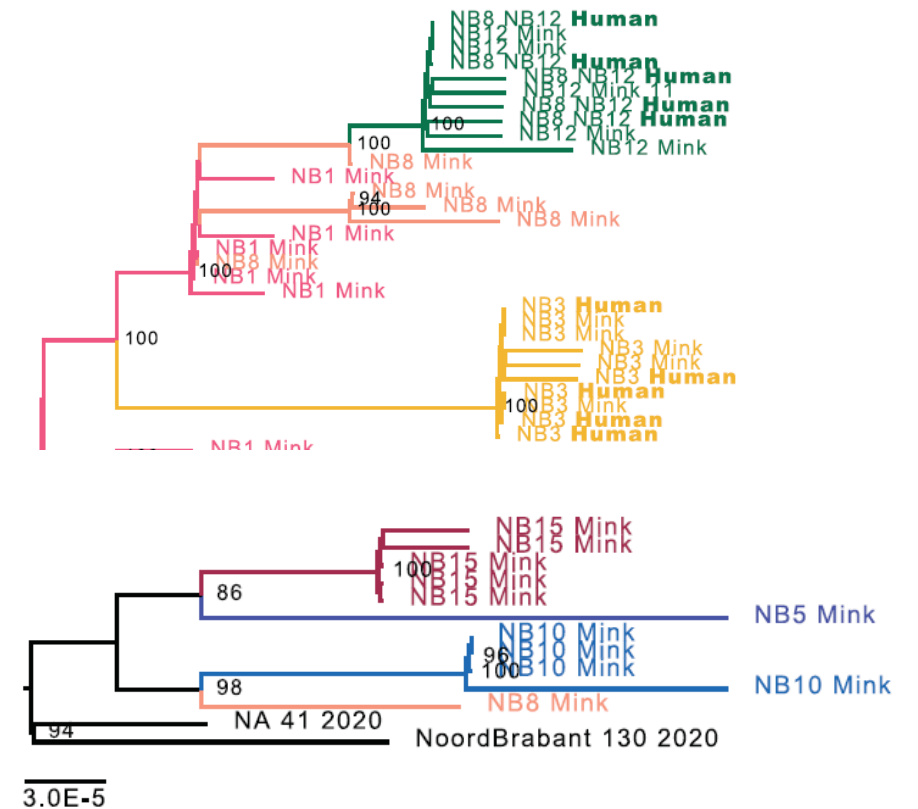
Source: Corman VM, et al, 2020. License: <https://creativecommons.org/licenses/by/4.0/legalcode>

## Application of WGS in Re-infection Cases

- 33 year old immunocompetent male
  - 1<sup>st</sup> diagnosis – March 26, 2020
  - 2<sup>nd</sup> diagnosis – (Ct value 26.7) Aug 15 returning from Spain
  - Patient was asymptomatic throughout the 2<sup>nd</sup> diagnosis
- Whole Genome Analysis:
  - 1st episode: stop codon in ORF – truncation of 58 AA
  - 23 nucleotide changes of which 13 are non-synonymous

# Transmission of SARS-CoV-2 between Mink and Farmers in the Netherlands

- Investigated outbreaks in 16 Mink farms in the Netherlands in Apr- May 2020
- WGS and epi investigation concluded transmission between humans and minks
- Many WGS strains had 0-9 nucleotide differences
- WGS of community strains showed significant difference



Source: Oude Munnink BB, et al, 2021. License: <https://creativecommons.org/licenses/by/4.0/legalcode>

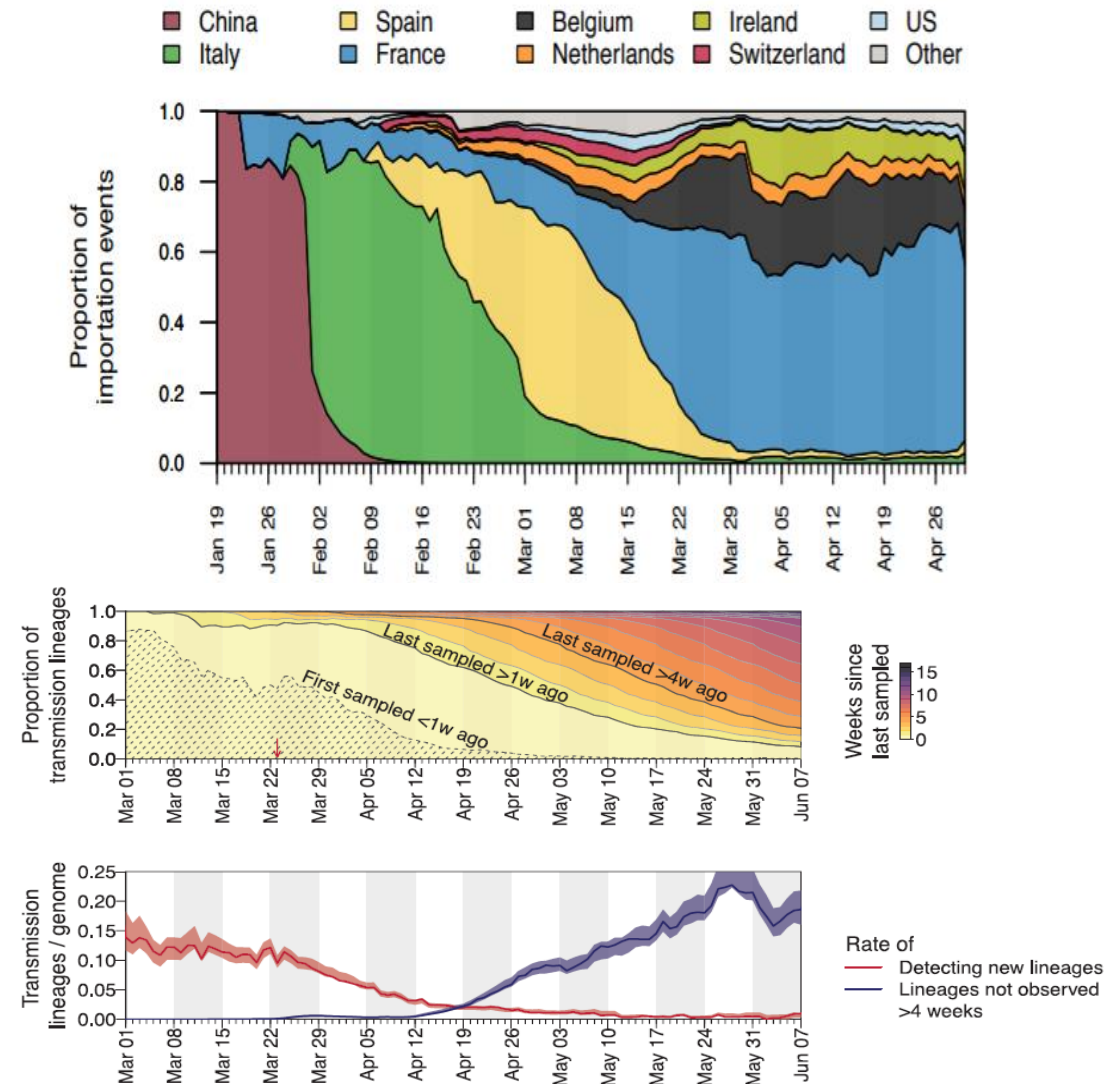
## Multi-Ward Outbreak of SARS-CoV-2 in March 2020

- Outbreak spanned March-April, 2020
  - 59 patients and 13 HCW
- WGS identified 6 separate clusters that when combined with epi data confirmed intra-hospital transmission
- Increased infection prevention and control interventions including universal surgical mask, screening, and testing led to control of outbreaks



# Establishment and lineage dynamics of the SARS-CoV-2 epidemic in the UK

- Demonstrated that WGS can be used to monitor viral emergence at the national level
- 26,000 samples were sequenced from Jan-June 2020
- Analysis was challenging due to limited sequence diversity
- Multiple importations from Europe led to establishment of SARS-CoV-2 in UK
- Most lineages disappeared over time



Source: du Plessis L, et al, 2021. License: <https://creativecommons.org/licenses/by/4.0/legalcode>

## Mutations and Lineages

- Mutations in the virus' genome sequence occur regularly and accumulate over time
- As mutations continue to accumulate, the genome becomes more different over time and can be called a new lineage
- New lineages may have “concerning” properties:
  - Increased virulence
  - Increased transmissibility
  - Evade natural or vaccine induced antibodies
  - Resistance to therapeutics (i.e. monoclonal antibody)
  - Affect diagnostic testing

World Health Organization, Genomic sequencing of SARS-CoV-2: a guide to implementation for maximum impact on public health, 2021

# Mutations and Lineages

- In early Dec 2020, the UK reported a specific lineage that made up 50% of cases in UK.
- Initially designated as variant under investigation (VUI)
- Mutation N501Y is one of six key contact residues within the receptor-binding domain (RBD) and has been identified as increasing binding affinity to human ACE2.
- Epidemiological, clinical and genomic data resulted in designation of this strain as Variant of Concern (VOC-202012/01) or B.1.1.7

Source: [www.outbreak.info](http://www.outbreak.info)

## Characteristic mutations of B.1.1.7

gene	amino acid
ORF1a	T100I
ORF1a	A1708D
ORF1a	I2230T
ORF1a	S3675K
ORF1a	del3676/3678
ORF1b	P314L
S	del69/70
S	del144/145
S	N501Y
S	A570D
S	D614G
S	P681H
S	T716I
S	S982A
S	D1118H
ORF8	Q27*
ORF8	R52I
ORF8	Y73C
N	D3L
N	R203K
N	G204R
N	S235F

## Dissemination of B.1.1.7 VOC

- First 2 cases identified in Canada on Dec 26, 2020 from Ontario
- Early Jan 2021 – large outbreak involving B.1.1.7 occurred with significant mortality
- By March, over 80% of cases were B.1.1.7

Public Health Ontario, COVID-19 variants of concern in Ontario: December 1, 2020 to May 9, 2021, 2021

# VOI/VOC Case Definitions

## Variant of Interest (VOI)

- Has a genome with mutations associated with changes in epidemiology, antigenicity, or virulence, or changes that *potentially* have a negative impact on available diagnostics, vaccines, therapeutics, or public health measures; **and**
- is known to cause community transmission/multiple COVID-19 cases/clusters in Canada or has been detected in multiple countries; **or**
- is otherwise assessed to be a VOI by WHO; **or**
- is otherwise assessed to be a VOI by the CSVSG.

## Variant of Concern (VOC)

- Through a comparative assessment, has been demonstrated to be associated with one or more of the following:
- increased transmissibility or detrimental change in COVID-19 epidemiology;
- increased virulence or change in clinical disease presentation;
- decreased effectiveness of available diagnostics, vaccines, therapeutics, or public health measures; **or**
- is otherwise assessed to be a VOC by WHO; **or**
- is otherwise assessed to be a VOC by the CSVSG.

## Notable mutations

- These lineage properties can be linked in part to notable mutations such as:
  - **N501Y:** A defining mutation in several lineages, including B.1.1.7 (Alpha), B.1.351 (Beta) and P.1 (Gamma). Increases binding to human cells
  - **E484K:** Appears in several lineages. May lead to reduced antibody neutralization
  - **K417N/T:** Appears in several lineages, including B.1.351 and P.1. May help the virus bind more tightly to cells
- PCR is a rapid means for identifying mutations that are known to be associated with VOC/VOI lineages but WGS is the only way that a VOC lineage can be identified

World Health Organization, Tracking SARS-CoV-2 variants, 2021

Griffiths E, et al, 2021

# Lineage Assignment

- There are many ways of classifying the different combinations of mutations in SARS-CoV-2 genomes into lineages
- The COVID-19 pandemic has largely relied on the Pango nomenclature system which uses statistical methods and epi criteria to determine when a combination of mutations is “different enough” to be considered its own lineage
- VOC lineages are more rigidly defined by notable mutations

## Pango lineage examples:

- AY.3
- B.1.1.7
- B.1.351
- B.1.617.2
- P.1.7



# SARS-CoV-2 genomics in Ontario

Test algorithms, specimen flows, and reporting



## Ontario COVID-19 Genomics Network

- The Ontario COVID-19 Genomics Network was established in March 2021 to increase genomics testing capacity in the province
- Includes 5 laboratories :
  - Public Health Ontario Laboratory
  - The Hospital for Sick Children
  - Shared Hospital Laboratory
  - Kingston Health Sciences Centre
  - Hamilton Regional Laboratory Medicine Program
- Routing of specimens from diagnostic to WGS labs is coordinated by Ontario Health

## Specimen Logistics

- SARS-CoV-2 diagnostic testing is provided by over 40 laboratories in the province including hospital, community, and public health laboratories
- All specimens positive for SARS-CoV-2 with a Ct value of  $\leq 35$  are sent to one of 11 VOC PCR testing laboratories for N501Y/E484K testing
- Select specimens with a Ct value of  $\leq 30$  on the VOC PCR are sent to one of the 5 Ontario COVID-19 Genomics Network laboratories for whole genome sequencing

Ontario Health, 2021

Public Health Ontario, SARS-CoV-2 (COVID-19 virus) variant of concern (VoC) surveillance, 2021

## What Specimens get WGS?

- Ct  $\leq$  30 to ensure there is enough genetic material in the specimen for sequencing
- Representative Sampling
  - As of May 2021, the Ontario COVID-19 Genomics Network started using a representative sampling framework for WGS
  - This replaced the previous approach of mostly sequencing based on the VOC PCR result to confirm lineages
  - The representative sampling allows for the relative proportions of each lineage circulating in Ontario to be monitored for changes
  - This approach also allows for the number of specimens sequenced to be scaled to the sequencing network's capacity of 3,500 specimens per week

European Centre for Disease Prevention and Control, 2021

## What Specimens get WGS?

- A proportion of all Ct eligible specimens tested for VOC PCR are selected randomly by the VOC PCR testing lab to forward for WGS
  - 10%-100% based on current and projected case counts
  - Also considers the proportion of all positives with eligible Ct values
- Notice of the proportion change is provided to VOC PCR labs 1 week in advance
  - Changes to sampling proportions announced at the Public Health Coordination Teleconference

## What Specimens get WGS?

- Targeted sampling - specimens are also sent for WGS when the requisition indicates:
  - International travel
  - Vaccine breakthrough
- Specimens collected as part of land border testing programs and day 8 airport testing are sequenced by the NML
- WGS is also available upon request to help support outbreak and suspected re-infection investigations through phylogenetic analysis (restrictions apply)

# WGS Representative Sampling Changes

- Initial implementation: Rise of the 3<sup>rd</sup> wave
  - PHO starts representative surveillance at 10% sample on May 2
  - OCGN starts representative surveillance at 10% sample on May 26
- First adjustment: Fall of the 3<sup>rd</sup> wave
  - PHO changes to 50% sample on May 30
  - OCGN changes to 50% sample on June 2
- Second adjustment: Inter-wave period
  - PHO and OCGN change to 100% sample on June 14
- Third adjustment: Rise of 4<sup>th</sup> wave
  - PHO and OCGN change to 50% sample on August 27

## Requesting WGS

- WGS results are for population level surveillance purposes and have limited use for individual clinical and public health management
  - Re-infection
  - IPAC cohorting
  - Outbreak management
- When proportional sampling is at 100% there is no need to request sequencing on specimens
- Representative and targeted sampling is only performed by VOC PCR testing laboratories and is not associated with the test request process

# Requesting WGS

- Requires requestor to arrange specimen be sent from VOC testing lab to WGS lab
- Specimens sent for WGS must be accompanied by the requisition found in the SARS-CoV-2 Variant of Concern Surveillance test information sheet
- For special requests additional information and approval may be required, please contact PHO Laboratory Incident Outbreak and Response Team prior to requesting WGS

Public Health Ontario | Santé publique Ontario

For laboratory use only  
PHO Laboratory No.: \_\_\_\_\_

### SARS-CoV-2 Variant of Concern Testing/ Whole Genome Sequencing Requisition

ALL sections of this form must be completed.

<p><b>1 - Indication for SARS-CoV-2 supplemental testing</b></p> <p><input type="radio"/> VOC mutation PCR testing requested<sup>1</sup> OR <input type="radio"/> Whole Genome Sequencing requested<sup>2</sup></p> <p>Below, please check all that apply.</p> <p><input type="checkbox"/> Representative Surveillance<sup>3</sup></p> <p><input type="checkbox"/> International travel - SARS-CoV-2 infection during international travel (including the United States) or within 14 days of entry to Canada (for routine WGS).<sup>4</sup></p> <p>Travel country / ies, specify: _____</p> <p><input type="checkbox"/> Vaccinated individuals with subsequent laboratory confirmed SARS-CoV-2 infection ≥14 days after receipt of vaccine (for routine WGS)<sup>5</sup></p> <p><input type="radio"/> After first dose of two dose series (partially vaccinated)</p> <p><input type="radio"/> After final dose (fully vaccinated)</p> <p><input type="checkbox"/> Outbreak / suspected super spreading event –two specimens per outbreak / event (for routine WGS).<sup>6</sup></p> <p><input type="checkbox"/> Other (Specify):<sup>7</sup> _____</p>	<p><b>2 - Patient Information<sup>8</sup></b></p> <p>Health Card No.: _____ Other unique ID#: _____</p> <p>Last Name: _____</p> <p>First Name: _____</p> <p>Date of Birth (yyyy/mm/dd): _____ Sex: <input type="radio"/> M <input type="radio"/> F</p> <p>Address: _____</p> <p>Postal Code: _____ Patient Phone No.: _____</p> <p>Investigation or Outbreak No.:<sup>9</sup> _____</p>
<p><b>5 - Special Requests</b> (For non routine requests only)</p> <p>If none of the indications for SARS-CoV-2 whole genome sequencing are met, contact PHO Laboratory Customer Service Centre at 1-877- 804-4567 or 416-235-6556 for testing approval for "Special request" prior to submission.</p> <p><input type="checkbox"/> Special request approved by Public Health Ontario:<sup>10</sup></p> <p><input type="checkbox"/> Suspected reinfection</p> <p><input type="checkbox"/> Outbreak specimens for phylogenetic analysis</p> <p><input type="checkbox"/> Other (Specify): _____</p> <p>WGS ID assigned:<sup>11</sup> _____</p> <p>Non-PHO lab specimen ID (if applicable): _____</p> <p>Provide details: _____</p> <p>Approving PHO Laboratory microbiologist: _____</p>	<p><b>3 - Specimen Location at Time of Request</b></p> <p><input type="radio"/> PHO Laboratory: if yes enter PHO Laboratory Specimen ID number: _____</p> <p>OR</p> <p><input type="radio"/> Non-PHO Laboratory:<sup>12</sup></p> <p>Submitting Lab director: _____</p> <p>Submitting Lab name: _____</p> <p>Submitting Lab address: _____</p> <p>CC: Requesting Authorized Healthcare Provider<sup>13</sup></p> <p>Name: _____</p> <p>OHIP   CPSO   Prof. License No.: _____</p> <p>Address: _____</p> <p>Fax number: _____</p> <p><b>4 - Specimen Information</b></p> <p>PCR gene target:<sup>14</sup> _____</p> <p>Submitting Lab specimen Ct value (required):<sup>15</sup> _____</p> <p>Date of SARS-CoV-2 positive test (yyyy/mm/dd): _____ (required)</p> <p>Collection Date (yyyy/mm/dd): _____</p> <p>Specimen Type (check all that apply):<sup>16</sup></p> <p><input type="checkbox"/> NPS <input type="checkbox"/> BAL</p> <p><input type="checkbox"/> Deep or Mid-turbinate Nasal Swab <input type="checkbox"/> Saliva (Spit &amp; Gargle)</p> <p><input type="checkbox"/> Oral (Buccal) + Deep Nasal <input type="checkbox"/> Saliva (Neat)</p> <p><input type="checkbox"/> Throat Swab <input type="checkbox"/> Anterior Nasal (Nose)</p> <p><input type="checkbox"/> Throat + Nasal <input type="checkbox"/> Other (Specify): _____</p>

Page 1 of 2, please turn the page for footnotes and additional notes on the reverse side of this form →

Source: Public Health Ontario, SARS-CoV-2 variant of concern testing / whole genome sequencing requisition, 2021  
Public Health Ontario, SARS-CoV-2 (COVID-19 virus) variant of concern (VoC) surveillance, 2021



## Requesting WGS: Outbreaks


- PHO is in the process of formalizing a centralized process for intake of WGS requests for outbreak support
  - Includes intake data and reporting templates
- Some outbreak specimens will be sequenced as part of the representative surveillance without requiring a request
- Additional specimens may be requested if lineage information will help support the response (e.g. suspected multiple introductions)
- In-depth phylogenetic analysis may also be requested if looking to test specific hypotheses about transmission (with limitations)

## WGS Reporting – Individual Patient Reports

- VOC lineages determined by WGS are reported to the ordering provider, PHU, and OLIS
  - Non-VOC lineages reported out as “Variant of Concern not detected”
  - VOC sub-lineages are reported out under the parent lineage (e.g. Delta sub-lineage AY.3 reported out as B.1.617.2)
- Non-VOC lineages are more dynamic and subject to re-classification which is problematic for “one-time” individual reports
- CCM logic to automatically populate lineage values from OLIS takes time to implement and cannot keep up with the emergence of new non-VOC lineages

## WGS Reporting – Aggregate Report


- PHO publishes a weekly WGS surveillance report on Fridays
- Includes VOC/VOI lineage proportions for Ontario overall and by PHU
- WGS results are linked to CCM to assign correct PHU and assess VOC/VOI lineage by outbreak status and disease severity

Updated 

SURVEILLANCE REPORT

**SARS-CoV-2 Whole Genome Sequencing in Ontario, August 18 2021**

This report summarizes the results of SARS-CoV-2 whole genome sequencing, including variants of concern (VOC) and variants of interest (VOI), conducted by the Ontario COVID-19 Genomics Network.

 1.7 MB | Updated 20 Aug 2021

Source: Public Health Ontario, SARS-CoV-2 Whole Genome Sequencing in Ontario, 2021

# WGS Reporting – Aggregate Report

**Table 1. Number of COVID-19 cases, number and percentage of cases sequenced for representative surveillance by week, Ontario, July 4 to July 31, 2021**

Week	Number of cases	Number sequenced	Percentage sequenced
Week 27 (July 4 to July 10)	1,299	780	60.0%
Week 28 (July 11 to July 17)	1,074	684	63.7%
Week 29 (July 18 to July 24)	1,099	686	62.4%
Week 30 (July 25 to July 31)	1,399	615	44.0%
Total	4,871	2,765	56.8%

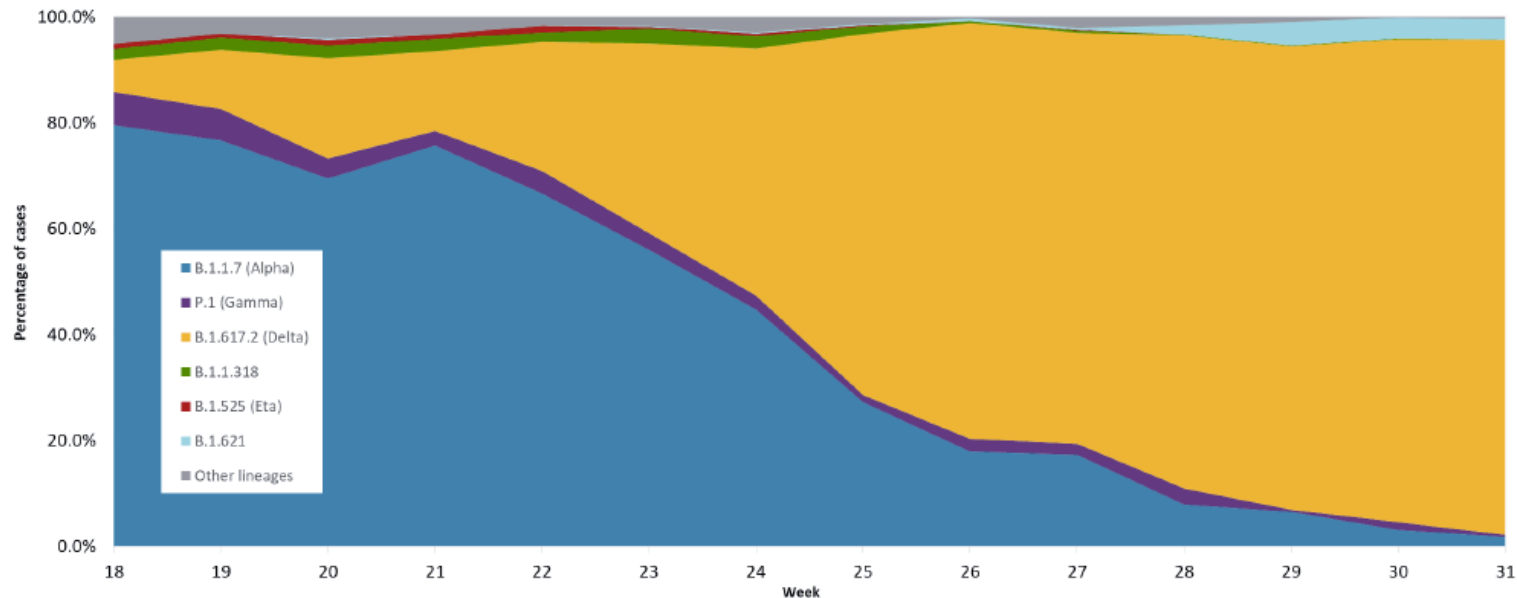
- Provides weekly breakdown of the proportion of cases sequenced
- May not align with current representative sampling proportions due to Ct eligibility requirements and data cut-off dates

Source: Public Health Ontario, SARS-CoV-2 whole genome sequencing in Ontario, 2021

# WGS Reporting – Aggregate Report

- Relative proportions of the 6 most common lineages (and other) by week since the start of representative sampling

Figure 1. Percentage of COVID-19 cases by top 6 most prevalent VOC/VOI lineages and week, representative surveillance, Ontario, May 2 to August 7, 2021



Source: Public Health Ontario, SARS-CoV-2 Whole Genome Sequencing in Ontario, 2021

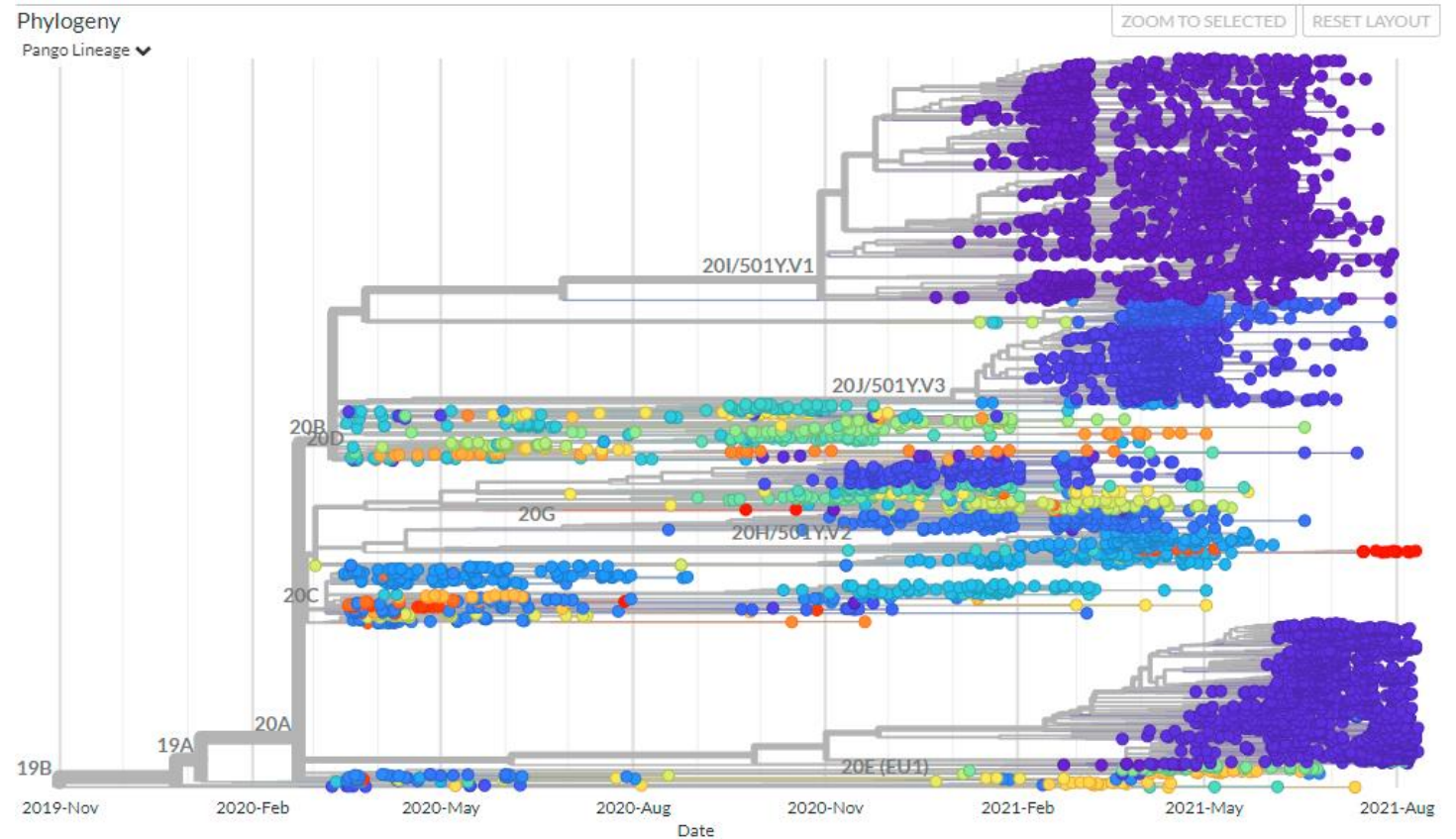
# WGS Reporting – Aggregate Report

**Table 5. Number and percentage (row %) of outbreak-associated and non outbreak-associated cases by VOC/VOI Pango lineage, representative surveillance, Ontario, July 4June 27 to July 2431, 2021**

Pango lineage (WHO label)	Outbreak-associated	Non outbreak-associated	Total cases
<b>Variant of concern</b>			
B.1.1.7 (Alpha)	46 (19.7%)	188 (80.3%)	234 (100%)
B.1.351 (Beta)	0 (0.0%)	2 (100%)	2 (100%)
P.1 (Gamma)	16 (34.8%)	30 (65.2%)	46 (100%)
B.1.617.2 (Delta)	261 (11.6%)	1,983 (88.4%)	2,244 (100%)
<b>Variant of interest</b>			
A.23.1	0 (0.0%)	0 (0.0%)	0 (0.0%)
B.1.1.318	0 (0.0%)	7 (100%)	7 (100%)
B.1.427/B.1.429 (Epsilon)	0 (0.0%)	0 (0.0%)	0 (0.0%)
B.1.525	0 (0.0%)	1 (100%)	1 (100%)
B.1.526 (Iota)	0 (0.0%)	1 (100%)	1 (100%)
B.1.616	0 (0.0%)	0 (0.0%)	0 (0.0%)
B.1.617.1 (Kappa)	0 (0.0%)	0 (0.0%)	0 (0.0%)
B.1.617.3	0 (0.0%)	0 (0.0%)	0 (0.0%)
B.1.621	14 (23.0%)	47 (77.0%)	61 (100%)
C.37 (Lambda)	0 (0.0%)	1 (100%)	1 (100%)
P.2 (Zeta)	0 (0.0%)	0 (0.0%)	0 (0.0%)
P.3 (Theta)	0 (0.0%)	0 (0.0%)	0 (0.0%)
<b>Non-VOC/VOI</b>	5 (13.5%)	32 (86.5%)	37 (100%)
<b>Total sequenced</b>	342 (13.0%)	2,292 (87.0%)	2,634 (100%)

Source: Public Health Ontario, SARS-CoV-2 Whole Genome Sequencing in Ontario, 2021

# NextStrain



- Shows a random 5,000 specimen sample of all cases sequenced by Public Health Ontario
- Contains all lineages (not just the VOC/VOI) and can be searched and filtered based on health region or lineage

Source: Public Health Ontario, Phylogenetic analysis of SARS-CoV-2 in Ontario, 2021

## Future Directions

- PHO is in the process of building a centralized sequence repository that will facilitate linking of all genomics network lab sequences to CCM and COVAX data
  - Interim processes for provincial surveillance reporting in place and are being continually enhanced
- Inclusion of additional travel information from border testing programs
- Weekly surveillance report to include VOC/VOI lineage by vaccination status
- Integration of additional sequencing technologies (Nanopore) to provide more flexible sequencing workflows



## References 1 of 5

- Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DKW, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill. 2020;25(3):2000045. Available from: <https://doi.org/10.2807/1560-7917.es.2020.25.3.2000045>
- du Plessis L, McCrone JT, Zarebski AE, Hill V, Ruis C, Gutierrez B, et al. Establishment and lineage dynamics of the SARS-CoV-2 epidemic in the UK. Science. 2021;371(6530):708-12. Available from: <https://doi.org/10.1126/science.abf2946>
- European Centre for Disease Prevention and Control. Guidance for representative and targeted genomic SARS-CoV-2 monitoring [Internet]. Stockholm: European Centre for Disease Prevention and Control; 2021 [cited 2021 Aug 31]. Available from: <https://www.ecdc.europa.eu/en/publications-data/guidance-representative-and-targeted-genomic-sars-cov-2-monitoring>
- Government of Canada. SARS-CoV-2 variants: national definitions, classifications and public health actions [Internet]. Ottawa, ON: Government of Canada; 2021 [cited 2021 Aug 31]. Available from: <https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/health-professionals/testing-diagnosing-case-reporting/sars-cov-2-variants-national-definitions-classifications-public-health-actions.html>

## References 2 of 5

- Griffiths E, Tanner J, Knox N, Hsiao W, Van Domselaar G; Canadian Public Health Laboratory Network; Canadian COVID-19 Genomics Network (CanCOGeN). CanCOGeN interim recommendations for naming, identifying, and reporting SARS-CoV-2 variants of concern [Internet]. Winnipeg, MB: Genome Canada; 2021 [cited 2021 Aug 31]. Available from: <https://nccid.ca/wp-content/uploads/sites/2/2021/02/CanCOGeN-Interim-Recommendations-for-Naming-Identifying-and-Reporting-SARS-CoV-2-Variants.pdf>
- Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. Nat Rev Microbiol. 2021;19(3):141-4. Available from: <https://doi.org/10.1038/s41579-020-00459-7>
- Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020;395(10224):565-74. Available from: [https://doi.org/10.1016/s0140-6736\(20\)30251-8](https://doi.org/10.1016/s0140-6736(20)30251-8)
- Lucey M, Macori G, Mullane N, Sutton-Fitzpatrick U, Gonzalez G, Coughlan S, et al. Whole-genome sequencing to track severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission in nosocomial outbreaks. Clin Infect Dis. 2021;72(11):e727-35. Available from: <https://doi.org/10.1093/cid/ciaa1433>

## References 3 of 5

- Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 variants of concern in Ontario: December 1, 2020 to May 9, 2021 [Internet]. Toronto, ON: Queen's Printer for Ontario; 2021 [cited 2021 Aug 31]. Available from: [https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-variant-epi-summary.pdf?sc\\_lang=en](https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-variant-epi-summary.pdf?sc_lang=en)
- Ontario Agency for Health Protection and Promotion (Public Health Ontario). Phylogenetic analysis of SARS-CoV-2 in Ontario [Internet]. Toronto, ON: Queen's Printer for Ontario; 2021 [cited 2021 Aug 31]. Available from: <https://www.publichealthontario.ca/en/data-and-analysis/infectious-disease/covid-19-data-surveillance/nextstrain#:~:text=This%20interactive%20tool%20supports%20genomics,diversity%20across%20the%20entire%20genome>
- Ontario Agency for Health Protection and Promotion (Public Health Ontario). SARS-CoV-2 (COVID-19 virus) variant of concern (VoC) surveillance [Internet]. Toronto, ON: Queen's Printer for Ontario; 2021 [cited 2021 Aug 31]. Available from: <https://www.publichealthontario.ca/en/laboratory-services/test-information-index/covid-19-voc>

## References 4 of 5

- Ontario Agency for Health Protection and Promotion (Public Health Ontario). SARS–CoV-2 variant of concern testing / whole genome sequencing requisition [Internet]. Toronto, ON: Queen’s Printer for Ontario; 2021 [cited 2021 Aug 31]. Available from: [https://www.publichealthontario.ca/-/media/documents/lab/sars-cov-2-voc-screening-request-form.pdf?sc\\_lang=en](https://www.publichealthontario.ca/-/media/documents/lab/sars-cov-2-voc-screening-request-form.pdf?sc_lang=en)
- Ontario Agency for Health Protection and Promotion (Public Health Ontario). SARS-CoV-2 whole genome sequencing in Ontario [Internet]. Toronto, ON: Queen’s Printer for Ontario; 2021 [cited 2021 Aug 31]. Available from: [https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-sars-cov2-whole-genome-sequencing-epi-summary.pdf?sc\\_lang=en](https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-sars-cov2-whole-genome-sequencing-epi-summary.pdf?sc_lang=en)
- Ontario Health. COVID-19 test collection and analysis [Internet]. Toronto, ON: Queen’s Printer for Ontario; 2021 [cited 2021 Aug 31]. Available from: <https://www.ontariohealth.ca/COVID-19/testing-analysis>
- Oude Munnink BB, Sikkema RS, Nieuwenhuijse DF, Molenaar RJ, Munger E, Molenkamp R, et al. Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans. *Science*. 2021;371(6525):172-7. Available from: <https://doi.org/10.1126/science.abe5901>

## References 5 of 5

- Rambaut A, Holmes EC, O’Toole Á, Hill V, McCrone JT, Ruis C, et al. A dynamic nomenclature proposal for SARS-CoV-2 lineages to assist genomic epidemiology. Nat Microbiol. 2020;5(11):1403-7. Available from: <https://doi.org/10.1038/s41564-020-0770-5>
- To KK, Hung IF, Ip JD, Chu AW, Chan WM, Tam AR, et al. COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. Clin Infect Dis. 2020 Aug 25 [Epub ahead of print]. Available from: <https://doi.org/10.1093/cid/ciaa1275>
- Wellcome Sanger Institute. COVID-19 genomic surveillance [Internet]. Cambridge: Wellcome Sanger Institute; 2021 [cited 2021 Aug 31]. Available from: <https://covid19.sanger.ac.uk/lineages/raw>
- World Health Organization. Genomic sequencing of SARS-CoV-2: a guide to implementation for maximum impact on public health. Geneva: World Health Organization; 2021. Available from: <https://www.who.int/publications/i/item/9789240018440>
- World Health Organization. Tracking SARS-CoV-2 variants [Internet]. Geneva: World Health Organization; 2021 [cited 2021 Aug 31]. Available from: <https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/>

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## Contact Information

Alex Marchand-Austin

[Alex.marchand-Austin@oahpp.ca](mailto:Alex.marchand-Austin@oahpp.ca)

Dr. Samir Patel

[Samir.Patel@oahpp.ca](mailto:Samir.Patel@oahpp.ca)