



THE HONG KONG
POLYTECHNIC UNIVERSITY
香港理工大學

Whole-genome sequencing of COVID-19 cases in Hong Kong: development of a geophylogenetic database and characterisation of SARS-CoV-2 variants circulating in the community (COVID190204)

Department of Health Technology and Informatics

Dr. Gilman K H SIU

Associate Professor, Limin Endowed Young Scholar

The Hong Kong Polytechnic University

Health Research Symposium

Construction of Geo-phylogenetic database of SARS-CoV-2



KWC

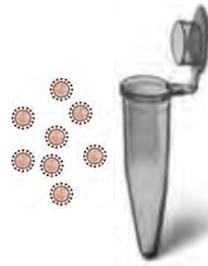
NTWC



HKEC

KEC

NTEC



Leftover total nucleic acid

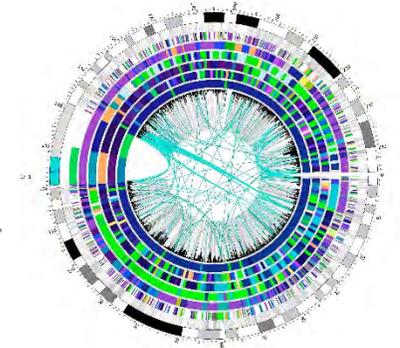
Illumina MiSeq (28 hrs)



Whole-genome Sequencing



Nanopore MinION / GridION (10 hrs)



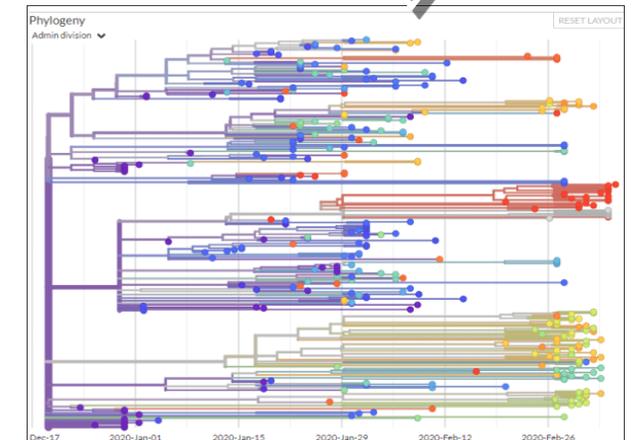
SARS-CoV-2 consensus genome

IQ-TREE

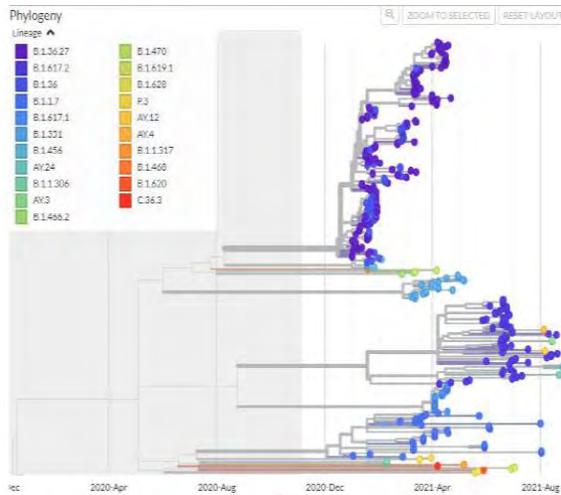
- Date of Confirmation
- Travel record
- Vaccination record

Nextstrain analysis workflow

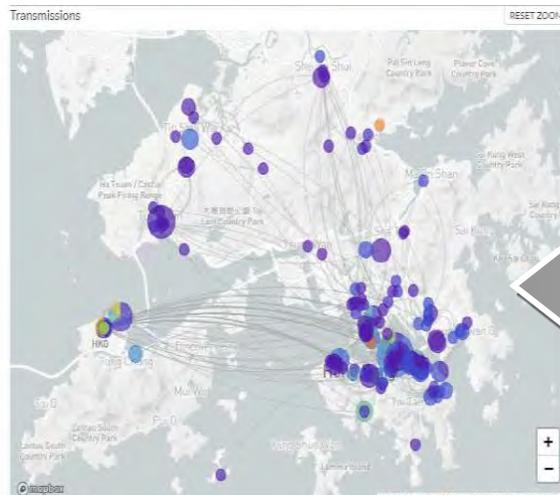
- Location of residence
- Location of visited places



Phylogenetic Tree



Time Tree

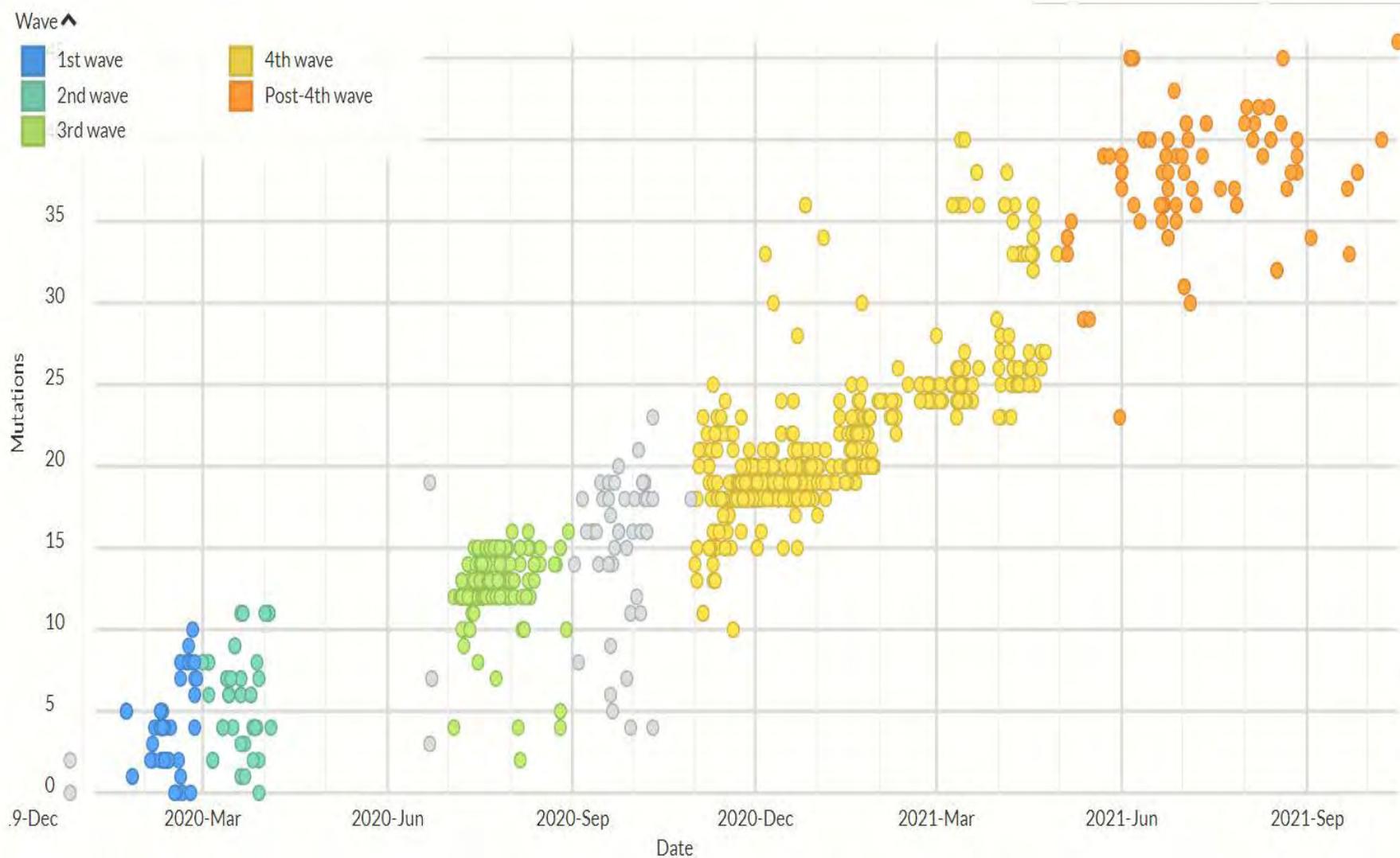
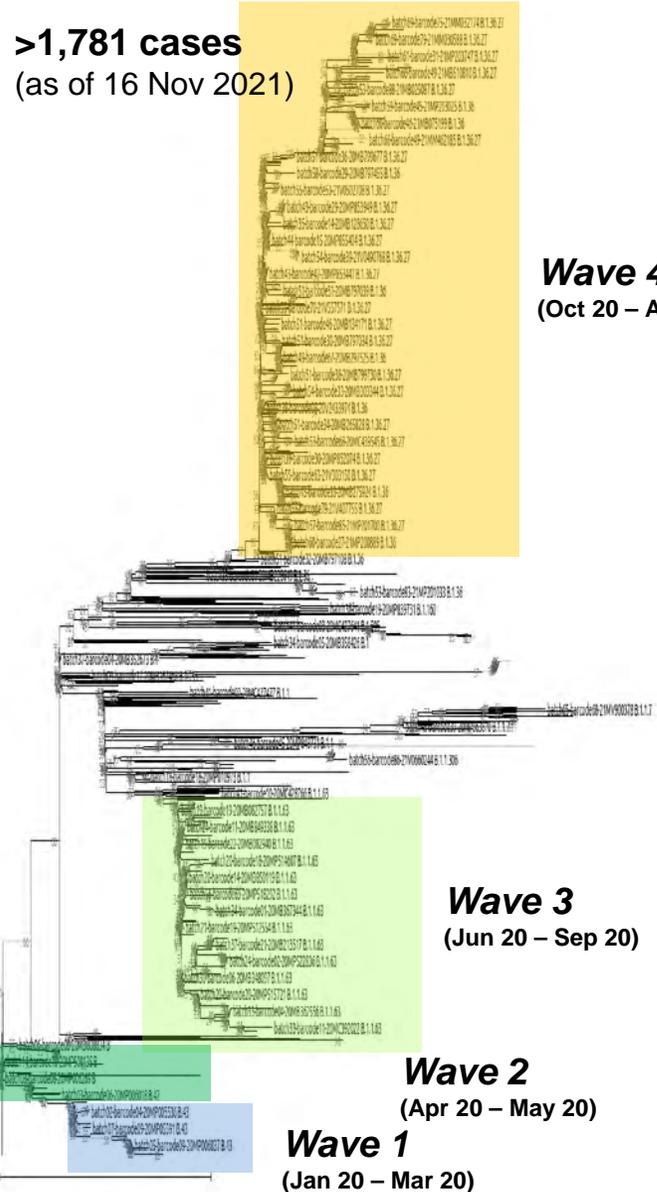


Interactive Map

Geo-phylogenetic Database

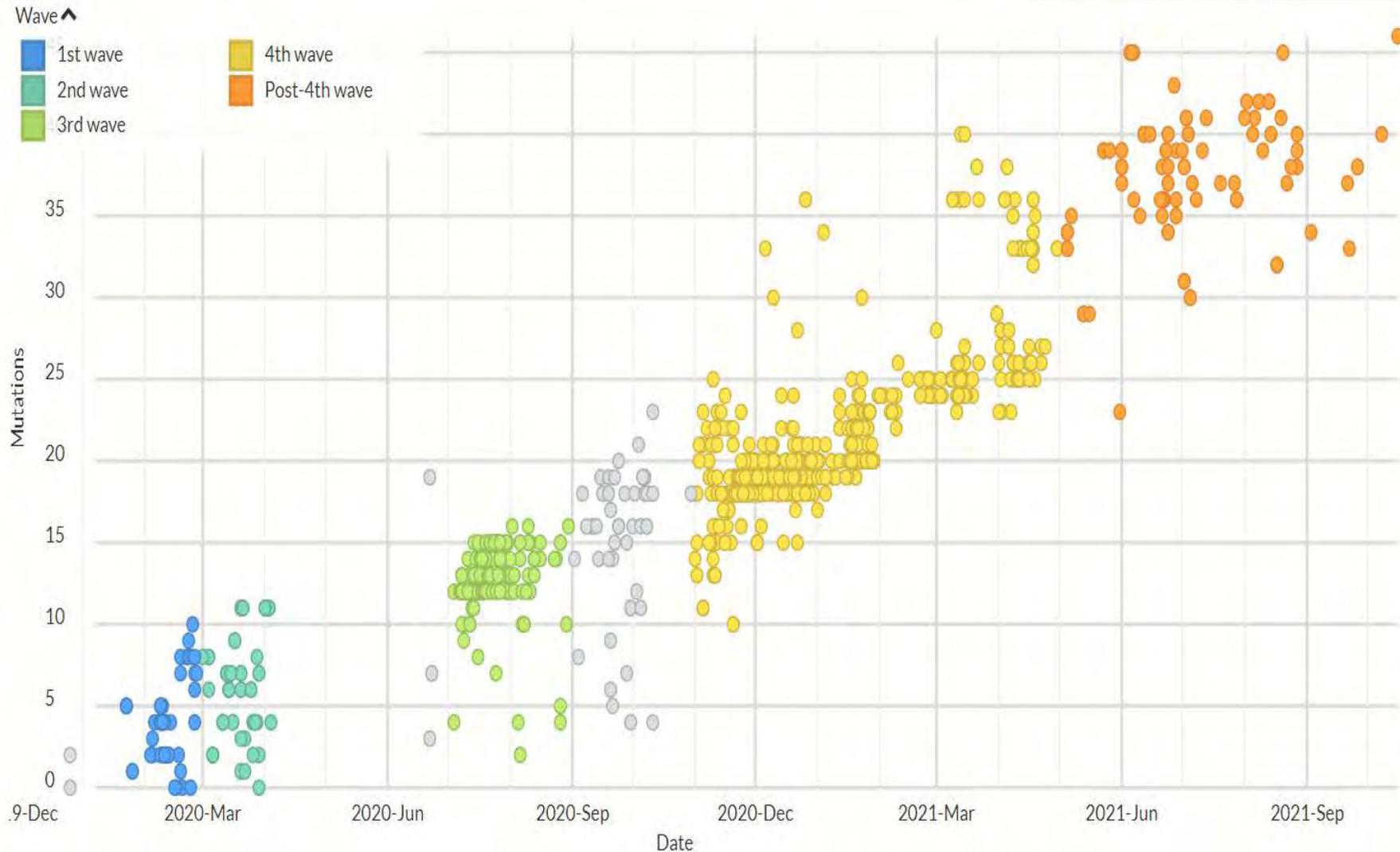
Conventional phylogeny and Evolution rate

>1,781 cases
(as of 16 Nov 2021)



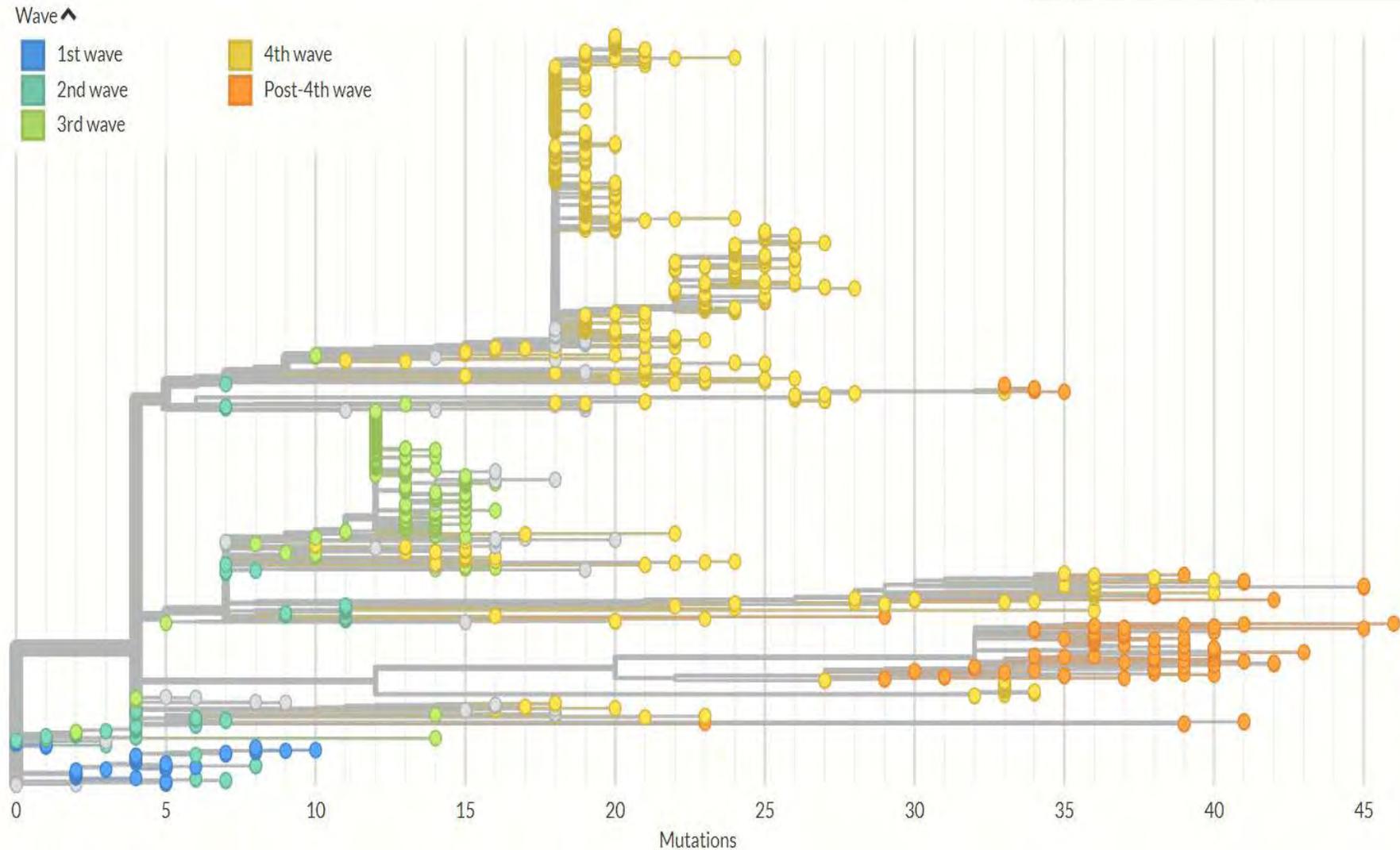
Construction of the “Time Tree”

- The number of mutation can be used as a ‘**molecular clock**’ to date the divergence between sequences.
- The tree was re-rooted to infer the internal nodes (ancestors).
- This tree demonstrates the phylogenetic relatedness and divergence of SARS-CoV-2 cases in Hong Kong

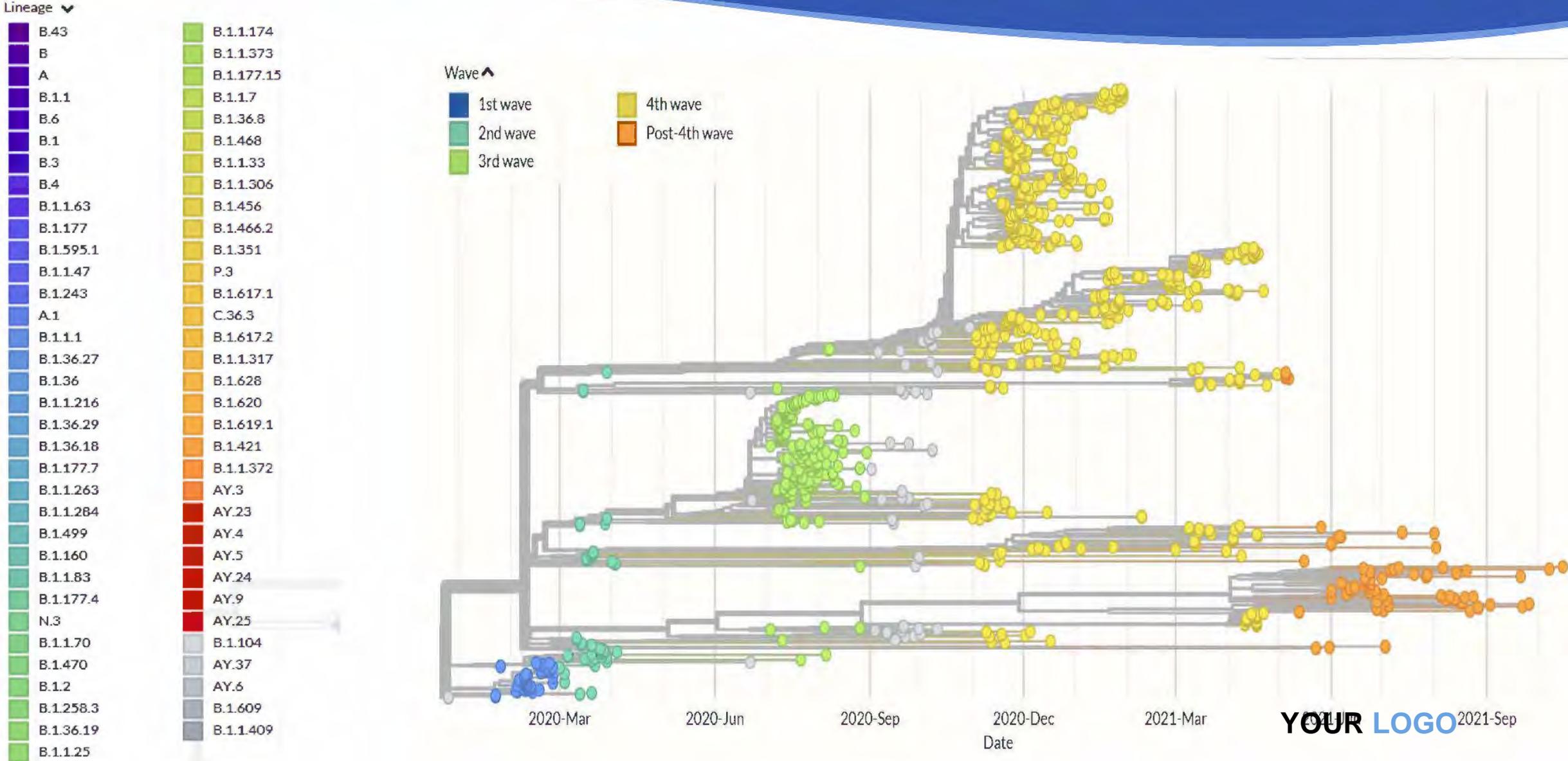


Construction of the “Time Tree”

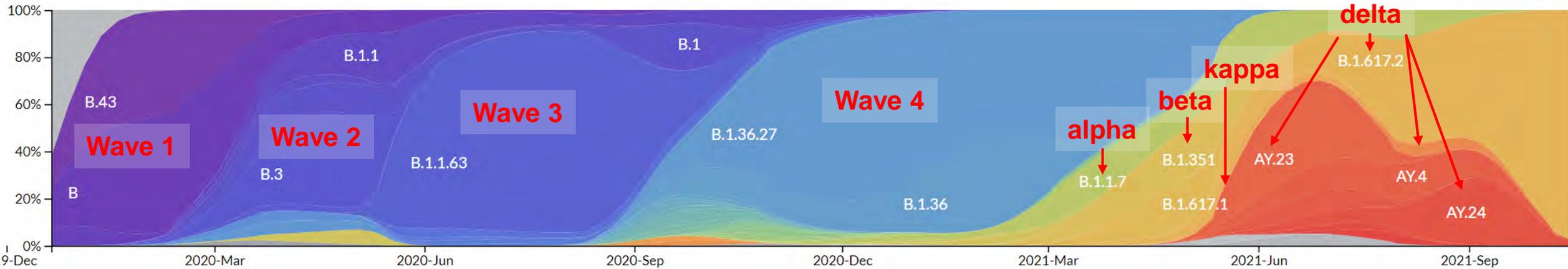
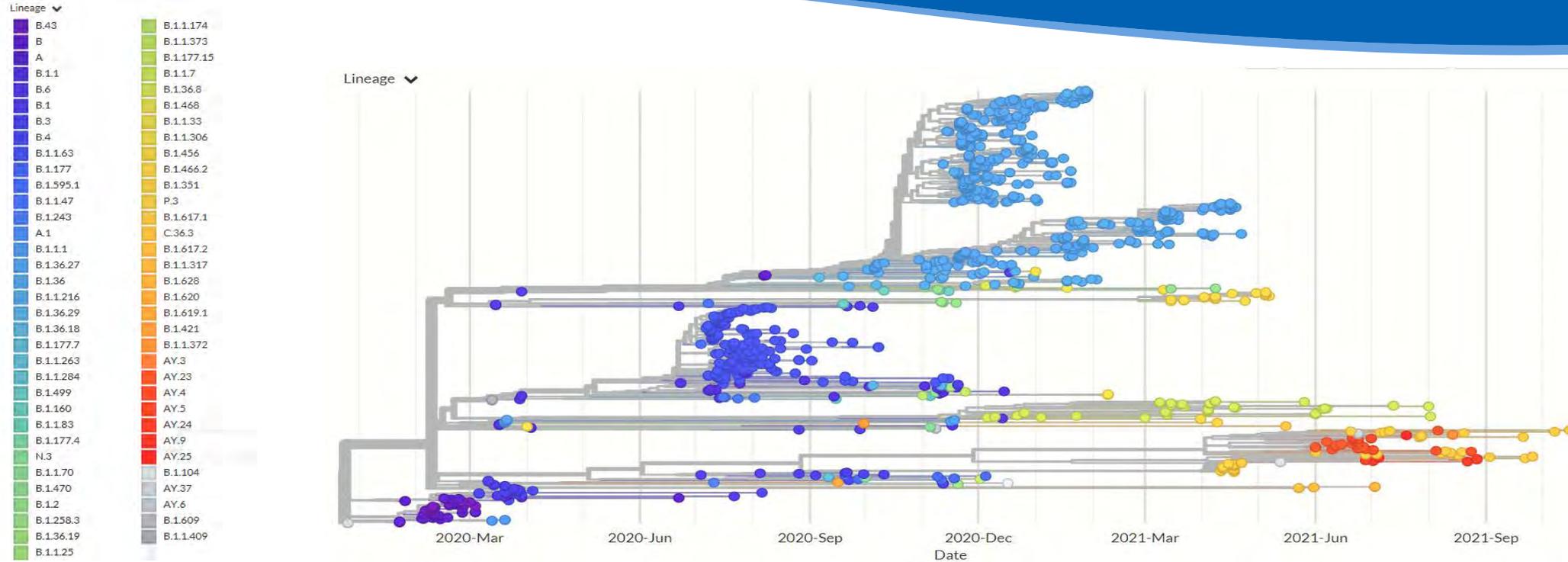
- The dates of case confirmation were added
- Branch lengths correspond directly to elapsed time
- Each node is placed such that its position reflects its known or inferred date.



Construction of the "Time Tree"



Frequency of SARS-CoV-2 lineages from 2020-2021



1st wave of outbreak (Jan – Feb 2020)

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

A-Z Index

Search



EMERGING INFECTIOUS DISEASES®

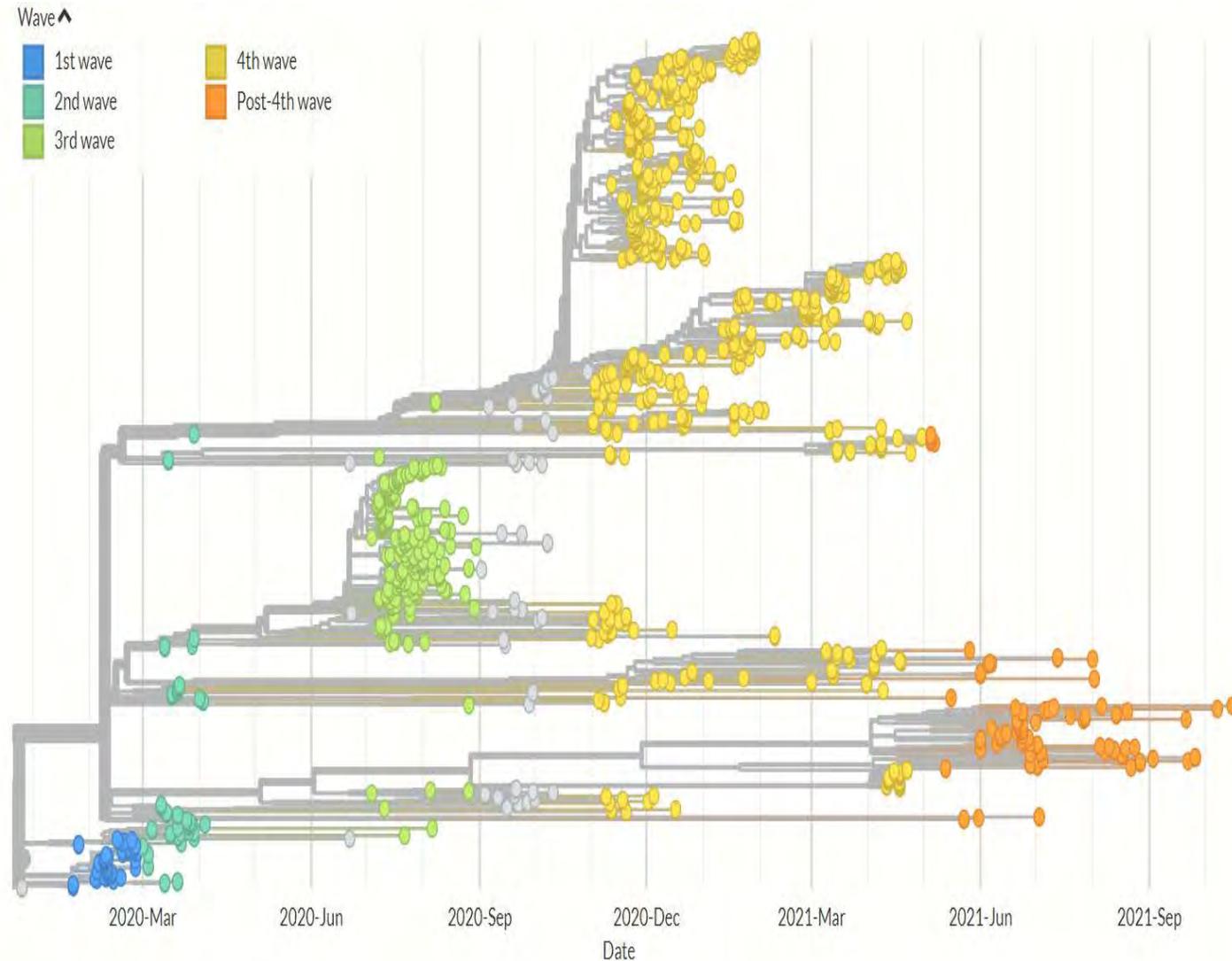
ISSN: 1080-6059

RESEARCH

Territorywide Study of Early Coronavirus Disease Outbreak, Hong Kong, China

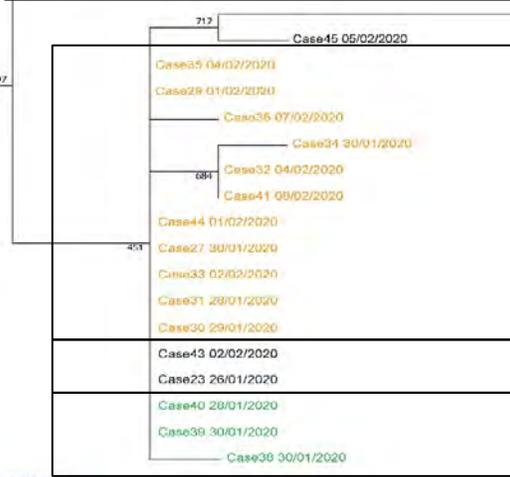
Kenneth Siu-Sing Leung, Timothy Ting-Leung Ng, Alan Ka-Lun Wu, Miranda Chong-Yee Yau, Hiu-Yin Lao, Ming-Pan Choi, Kingsley King-Gee Tam, Lam-Kwong Lee, Barry Kin-Chung Wong, Alex Yat-Man Ho, Kam-Tong Yip, Kwok-Cheung Lung, Raymond Wai-To Liu, Eugene Yuk-Keung Tso, Wai-Shing Leung, Man-Chun Chan, Yuk-Yung Ng, Kit-Man Sin, Kitty Sau-Chun Fung, Sandy Ka-Yee Chau, Wing-Kin To, Tak-Lun Que, David Ho-Keung Shum, Shea Ping Yip, Wing Cheong Yam, Gilman Kit-Hang Siu

- 50 cases of SARS-CoV-2 infections
- 8 imported cases
- 42 locally-acquired cases
 - Hotpot cluster
 - Cheung Hong Estate / Star Seafood restaurant
 - Mahjong Family
 - Taikoo Shing Engineer Family
 - Buddha Worship Hall





Buddha
Worship
hall



Hotpot cluster

Sporadic cases in Eastern district

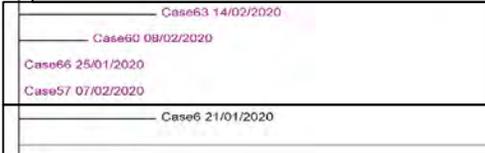
Mahjong family



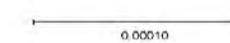
Cheung Hong Estate /
Star Seafood Restaurant

Taikoo Shing Engineer

Imported cases



NC_045512 China ← First SARS-CoV-2 genome



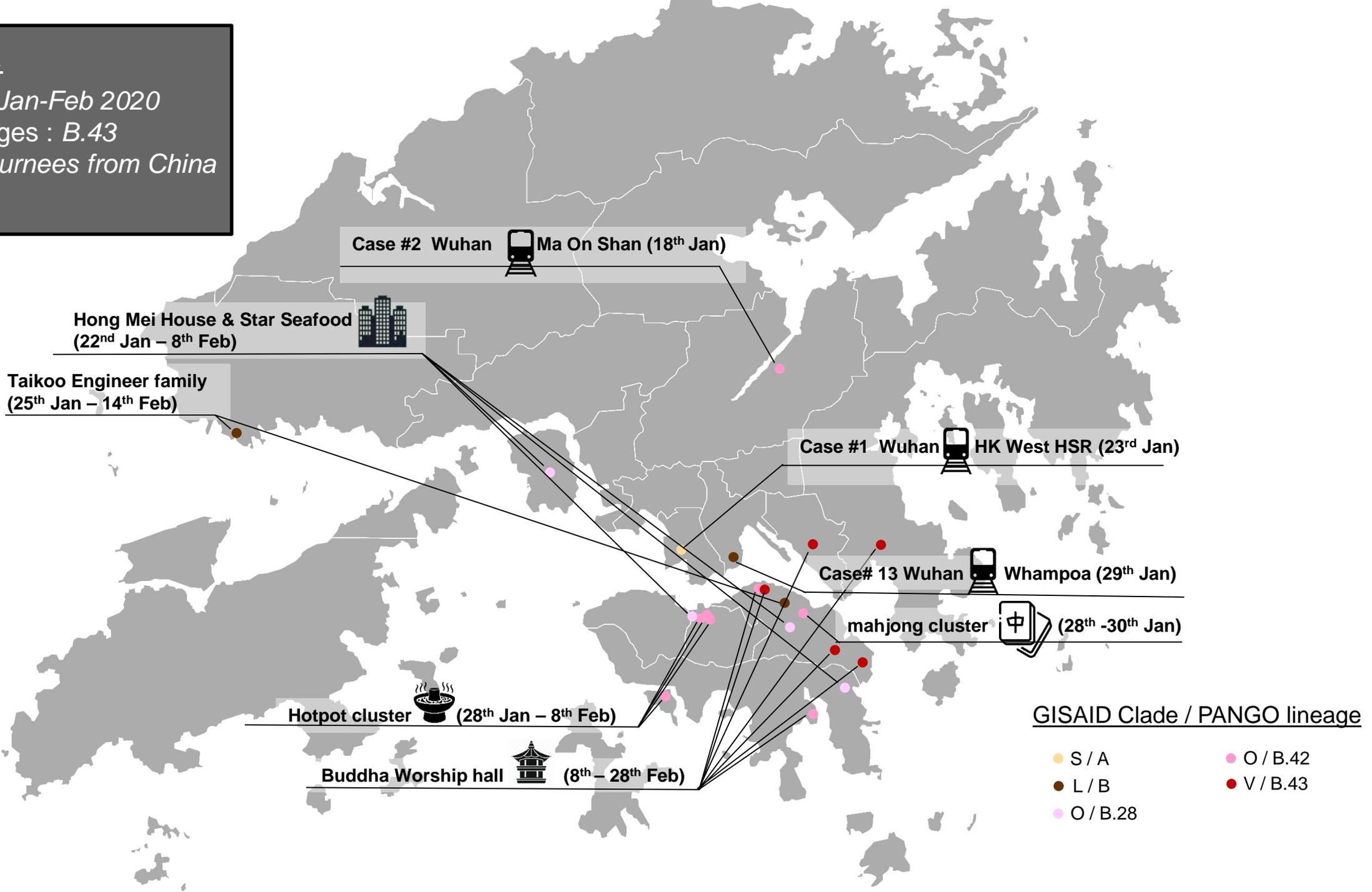
- Phylogenetic clustering highly concordant to the epidemiological investigation
- Multiple cases in Eastern District were likely caused by a single source → Hidden transmission chain
- Identified the potential source of the Buddha Worship Hall cluster
- Demonstrated the possibility of “hidden spreader” as a source of COVID-19 community outbreak.

Wave 1

Time point: *Jan-Feb 2020*

Major Lineages : *B.43*

Source: *Returnees from China*



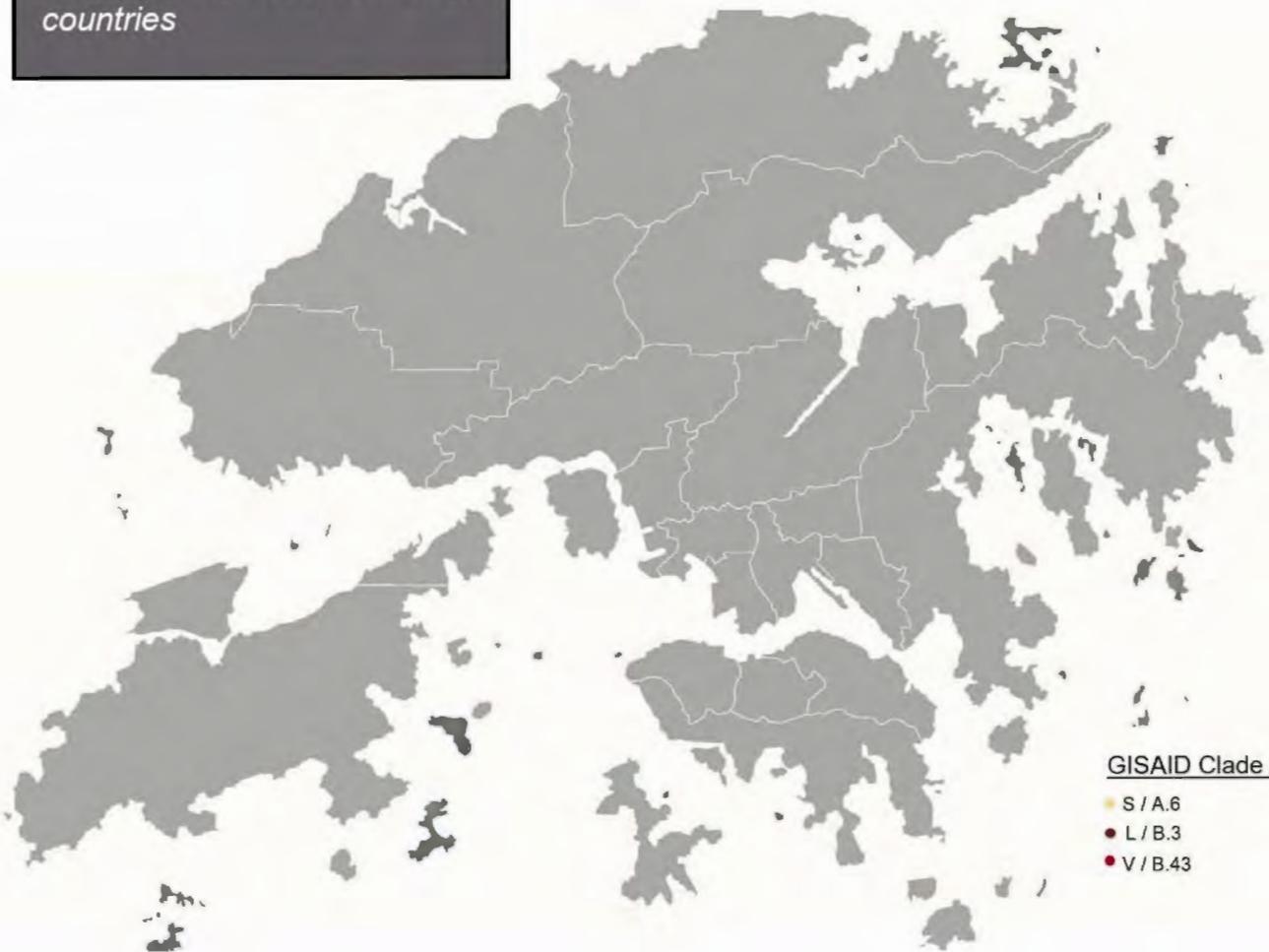
2nd wave of outbreak (Mar – Apr 2020)

Wave 2

Time point: *Mar-Apr 2020*

Major Lineage : *B.1, B.3*

Source: *Returns from Other countries*

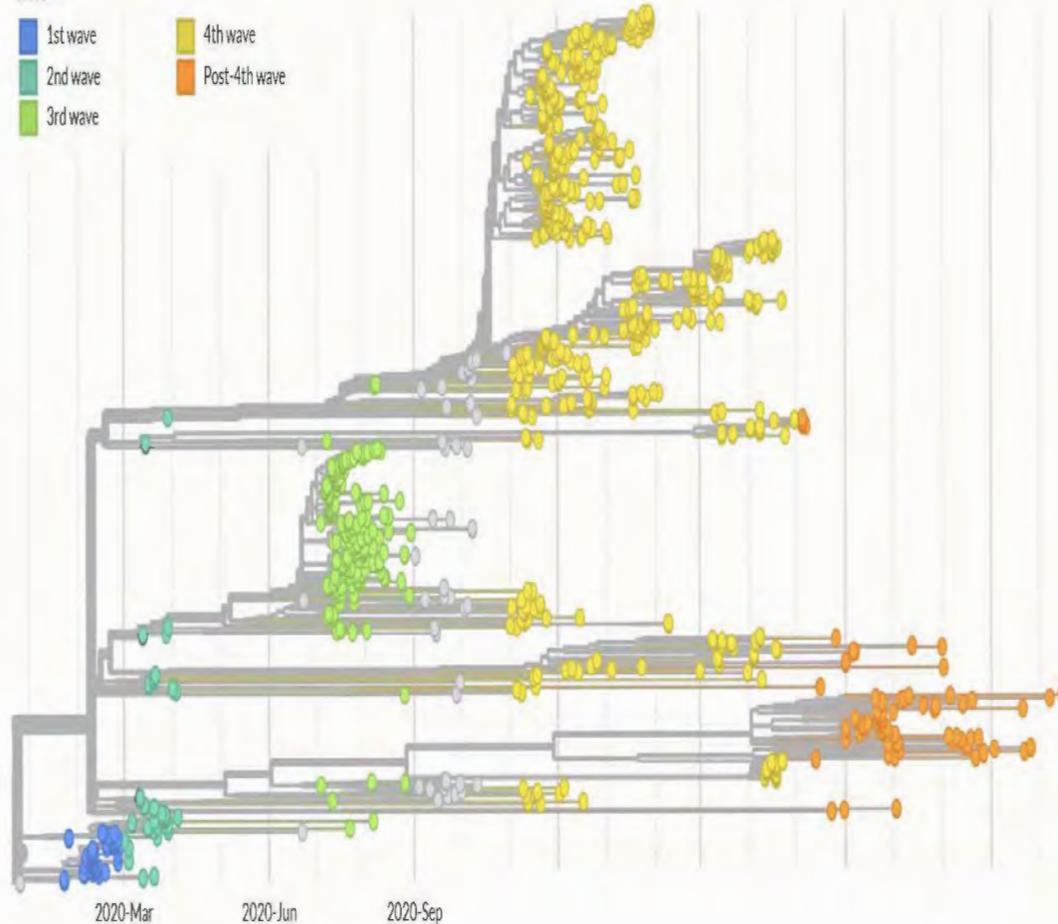


GISAID Clade / PANGO lineage

- S / A.6
- L / B.3
- V / B.43
- G / B.1
- G / B.1.1.28
- G / B.1.153
- GR / B.1.177

Wave ▲

- 1st wave
- 2nd wave
- 3rd wave
- 4th wave
- Post-4th wave

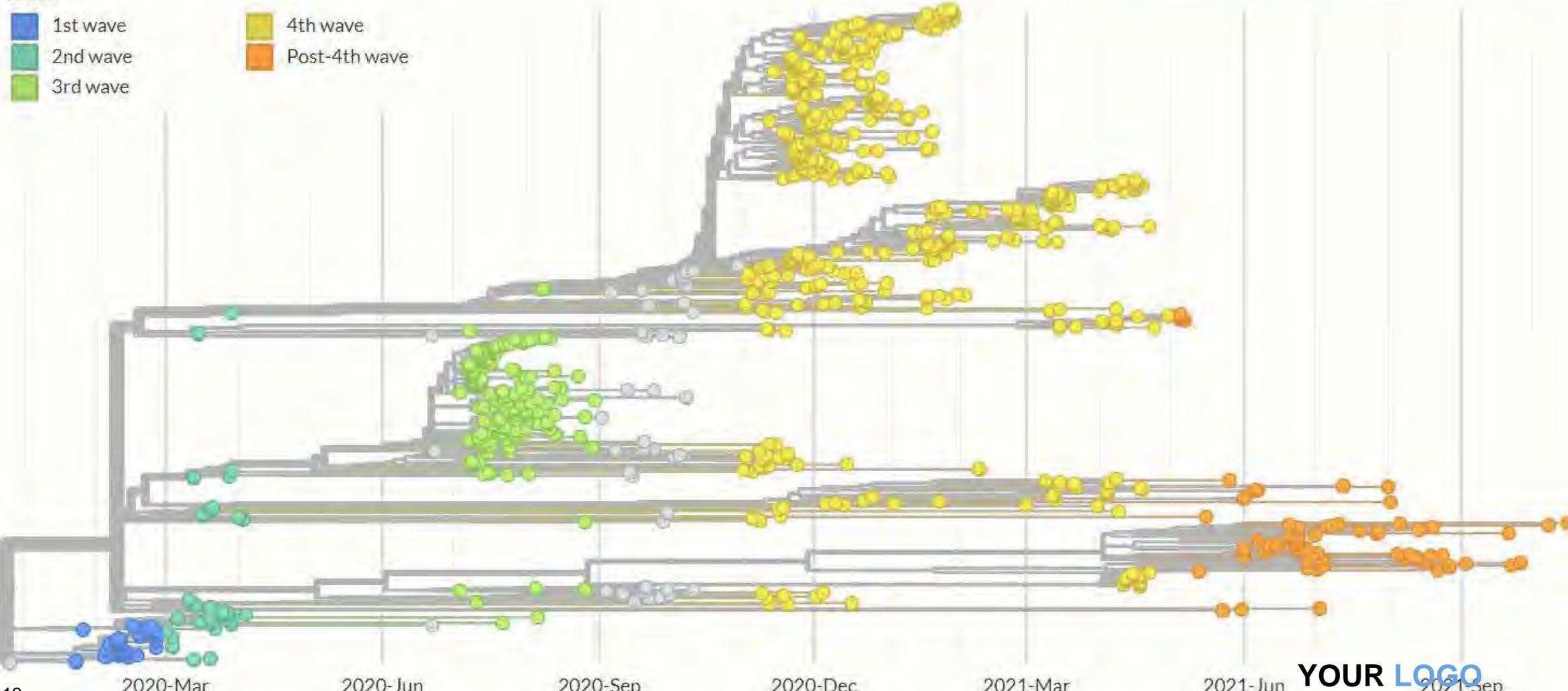


YOUR LOGO

3rd wave of outbreak (Jul – Sept 2020)

Wave ^

- 1st wave
- 2nd wave
- 3rd wave
- 4th wave
- Post-4th wave



Government suspended unrestricted crew changes in July 2020

Coronavirus pandemic

FOLLOW

Hong Kong / Health & Environment

Hong Kong third wave: as more sailors confirmed with Covid-19, experts call for suspension of unrestricted crew changes

- 'If a group has come in [from other places], but quarantine is not imposed on them ... this will only lead to sustained entry of the virus': government adviser
- According to the Marine Department, about 10,000 sea crew members have been granted quarantine exemption to date



Elizabeth Cheung and Victor Ting

Published: 10:15pm, 24 Jul, 2020

Why you can trust SCMP

TOP PICKS

Choosing the Right Secondary School

Paid Post: Stamford American School HK



Coronavirus 'Grim situation' as Hong Kong records first local untraceable Covid-19 mutant case

30 Apr 2021



News Cathay Pacific offers Hong Kong pilots, cabin crew voluntary redundancy

29 Apr 2021



1.3k



YOUR LOGO

Pre-Wave 4

Time point: 25 Sept - 10 Oct

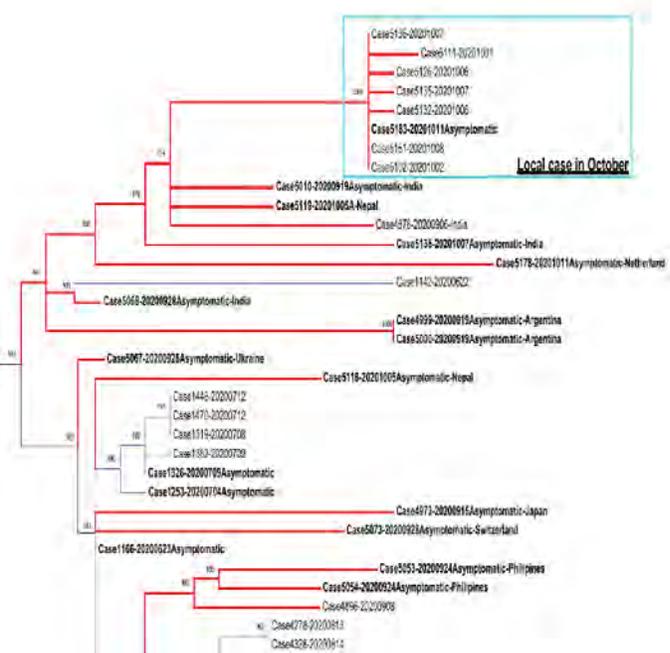
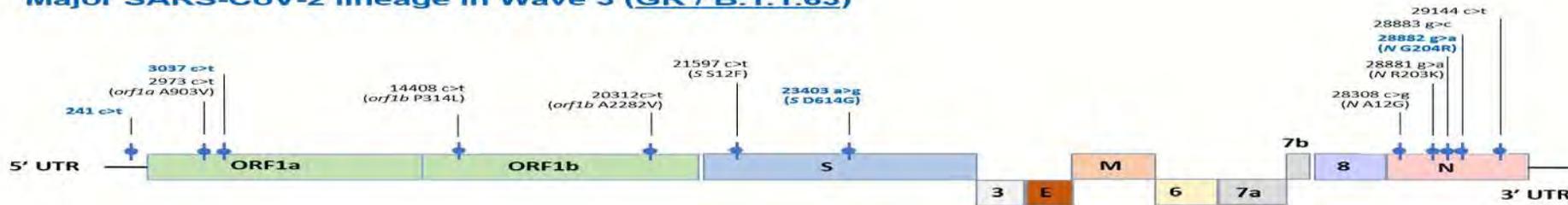
Major Lineage : **B.1.36.27**

Source: *Imported case from Nepal*

Local cases ● Imported cases ★

GH / B.1.36.27 ● ★

Major SARS-CoV-2 lineage in Wave 3 (GR / B.1.1.63)



Pre- 4th Wave of Outbreak (Sept – Oct 2020)

- Under the 14-day compulsory quarantine arrangement, persons must stay in their pre-arranged quarantine premises (in hotel rooms) at all times
- Although electronic wristbands are arranged to monitor travellers' location, they can still be visited by or even dined with their families or friends at the hotel rooms.
- Visitors may be infected and spread the virus in the community



LETTER



Will a new clade of SARS-CoV-2 imported into the community spark a fourth wave of the COVID-19 outbreak in Hong Kong?

Gilman Kit-Hang Siu ^{a#}, Lam-Kwong Lee^{a#}, Kenneth Siu-Sing Leung^{b#}, Jake Siu-Lun Leung^a, Timothy Ting-Leung Ng^a, Chloe Toi-Mei Chan^a, Kingsley King-Gee Tam^b, Hiu-Yin Lao^a, Alan Ka-Lun Wu^c, Miranda Chong-Yee Yau^c, Yvette Wai-Man Lai^c, Kitty Sau-Chun Fung^d, Sandy Ka-Yee Chau^d, Barry Kin-Chung Wong^d, Wing-Kin To^e, Kristine Luk^e, Alex Yat-Man Ho^e, Tak-Lun Que^f, Kam-Tong Yip^f, Wing Cheong Yam^b, David Ho-Keung Shum^g and Shea Ping Yip ^a

^aDepartment of Health Technology and Informatics, The Hong Kong Polytechnic University, Hung Hom, Hong Kong Special Administrative Region, People's Republic of China; ^bDepartment of Microbiology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Pokfulam, Hong Kong Special Administrative Region, People's Republic of China; ^cDepartment of Clinical Pathology, Pamela Youde Nethersole Eastern Hospital, Chai Wan, Hong Kong Special Administrative Region, People's Republic of China; ^dDepartment of Clinical Pathology, United Christian Hospital, Kwun Tong, Hong Kong Special Administrative Region, People's Republic of China; ^eDepartment of Pathology, Princess Margaret Hospital, Kwai Chung, Hong Kong Special Administrative Region, People's Republic of China; ^fDepartment of Clinical Pathology, Tuen Mun Hospital, Tuen Mun, Hong Kong Special Administrative Region, People's Republic of China; ^gFaculty of Health and Social Science, The Hong Kong Polytechnic University, Hung Hom, Hong Kong Special Administrative Region, People's Republic of China

ARTICLE HISTORY Received 16 October 2020; Revised 4 November 2020; Accepted 8 November 2020

KEYWORDS COVID-19; SARS-CoV-2; whole genome sequencing; Phylogeny; outbreak

> a, 6255c > t (*Orf1a* A1997V), 7504c > t, 18,877c > t, 22,444c > t, 24,175t > c, 26,060c > t (*Orf3a* T223I), 26,735c > t, and 28,854c > t (*N* S194L). Notably, the new genomes differ from those in the third wave by at least 22 nucleotides (Supplementary Figure 2). Based on our previous study [1], the average evolutionary rate of SARS-CoV-2 was 3.04×10^{-3} substitutions per site per year, meaning that the virus may accumulate about 7.6 nucleotide changes per month. The significant variations in the genomes might indicate that the new SARS-CoV-2 variants are unlikely to evolve

As many parts in the world are experiencing a new wave of infections with exponentially increased confirmed cases, the city's border control measures are needed to be strengthened to prevent imported infections. It would seem advisable to elevate the testing and quarantine arrangement for passengers from low-risk places to the same level as for those from high-risk places. During the 14-day compulsory quarantine, travellers would be better to stay in the quarantine centres or hotels designated by the Government, where visitors are not allowed.

Of particular concern is a recent much-touted plan

4th wave of outbreak (Nov 2020 – April 2021)

Wave 4

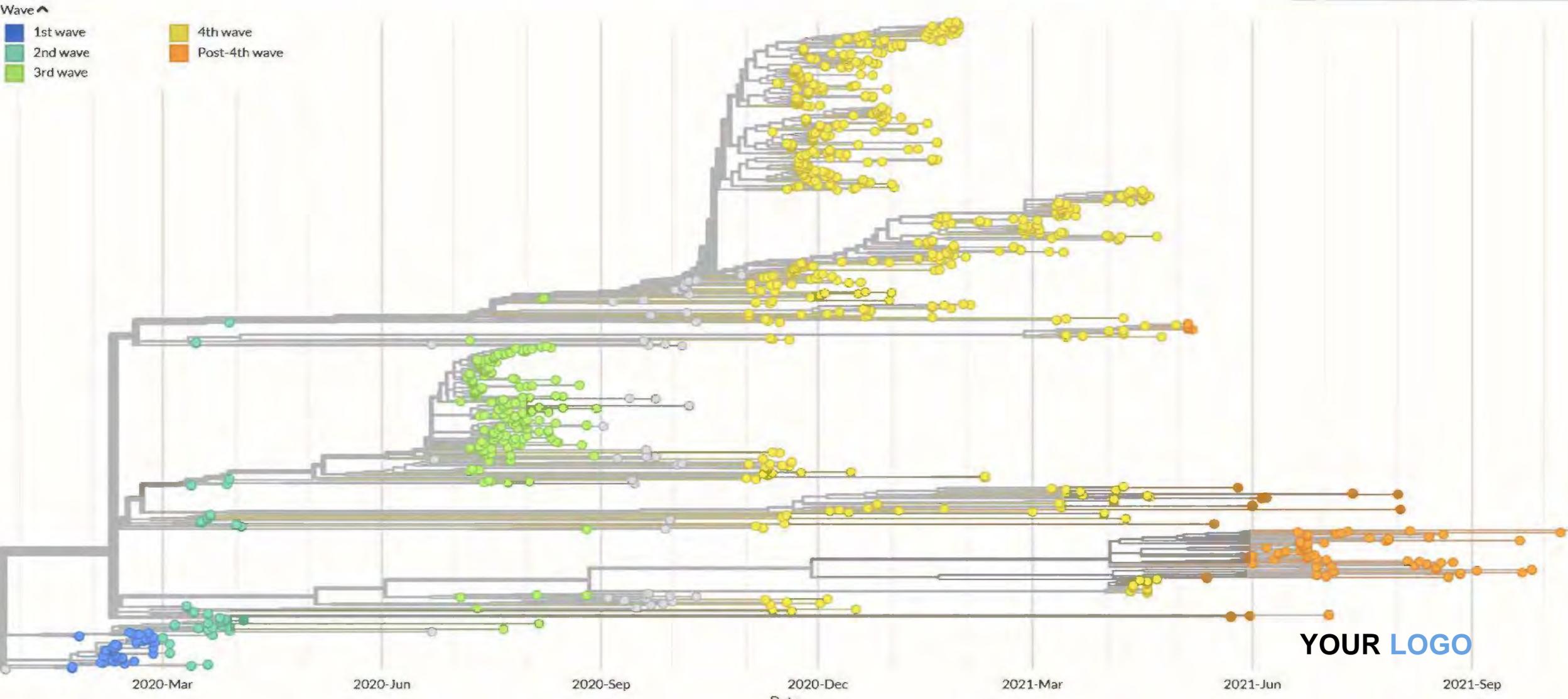
Time point: 19 Nov 2020 – 21 April 2021

Major Lineage : **B.1.36.27**

Source: *Dancing cluster* (n=736)

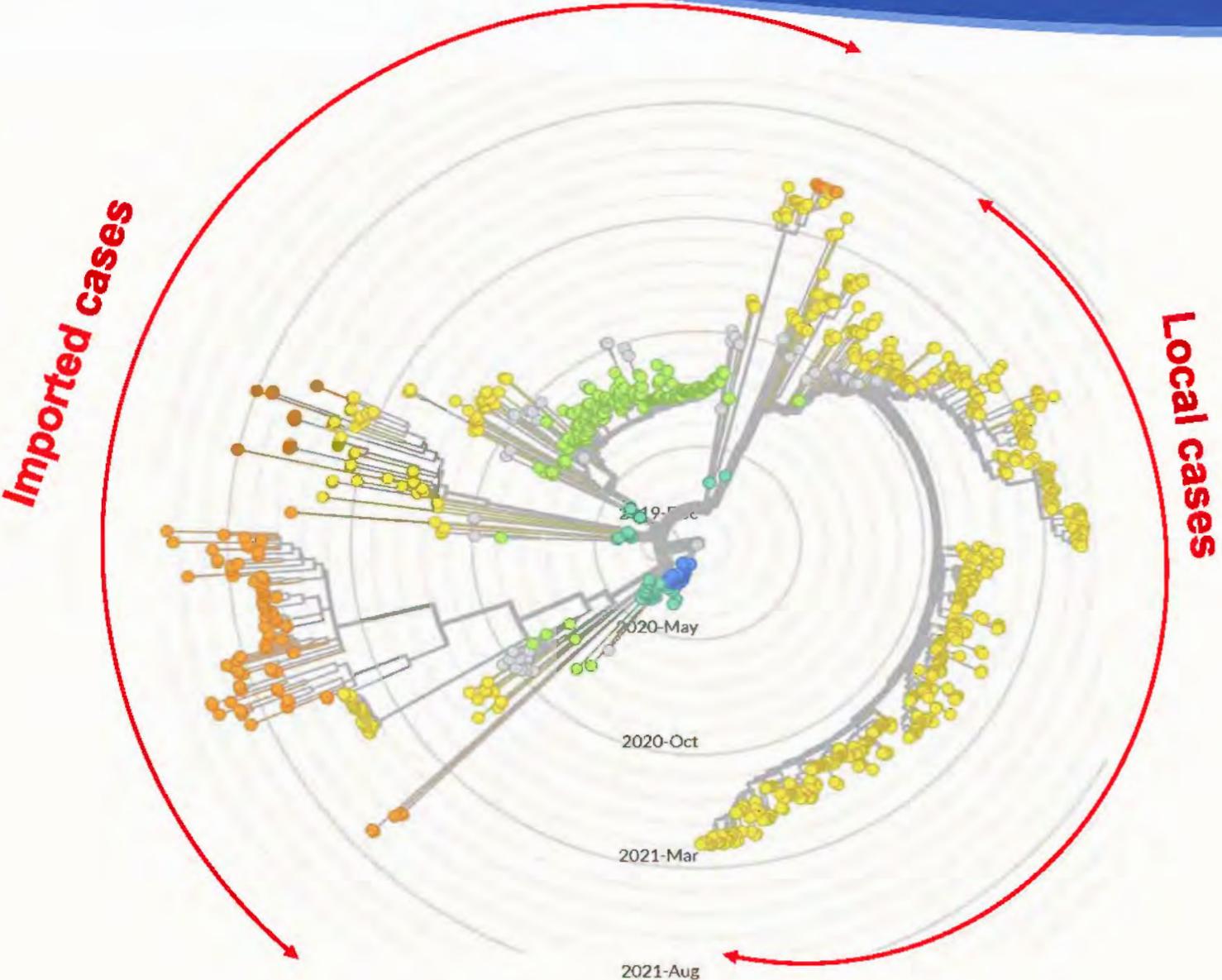


4th wave of outbreak (Nov 2020 – April 2021)



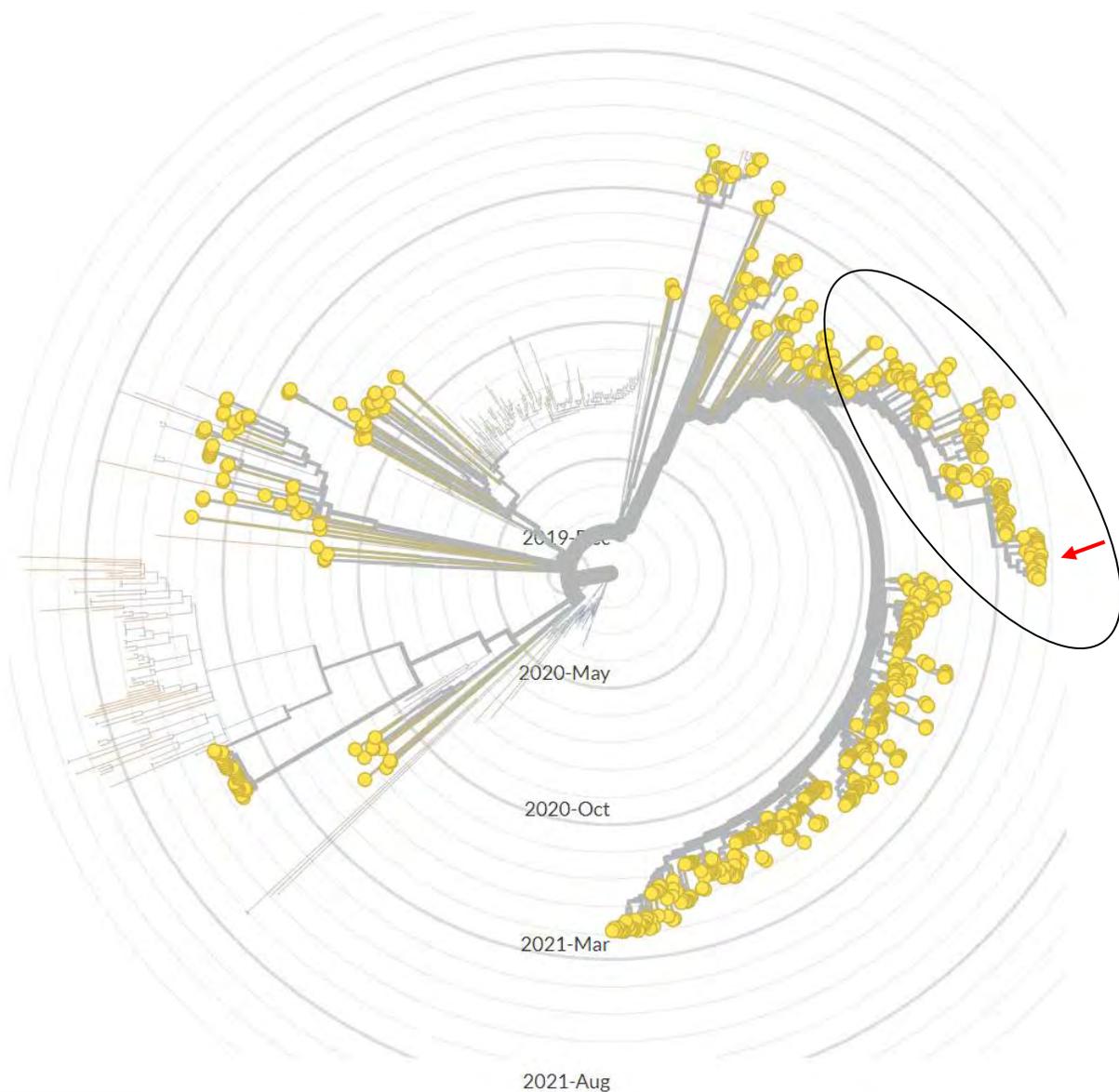
4th wave of outbreak (Nov 2020 – April 2021)

- Wave ^
- 1st wave
 - 2nd wave
 - 3rd wave
 - 4th wave
 - Post-4th wave



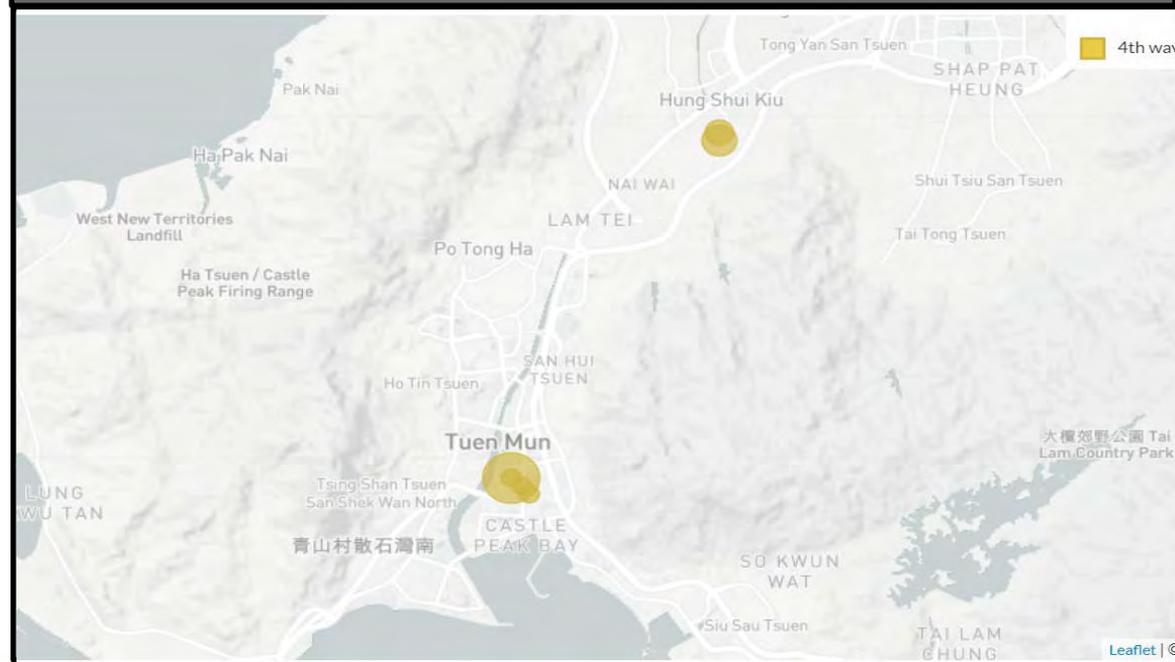
YOUR LOGO

4th wave of outbreak (Nov 2020 – April 2021)

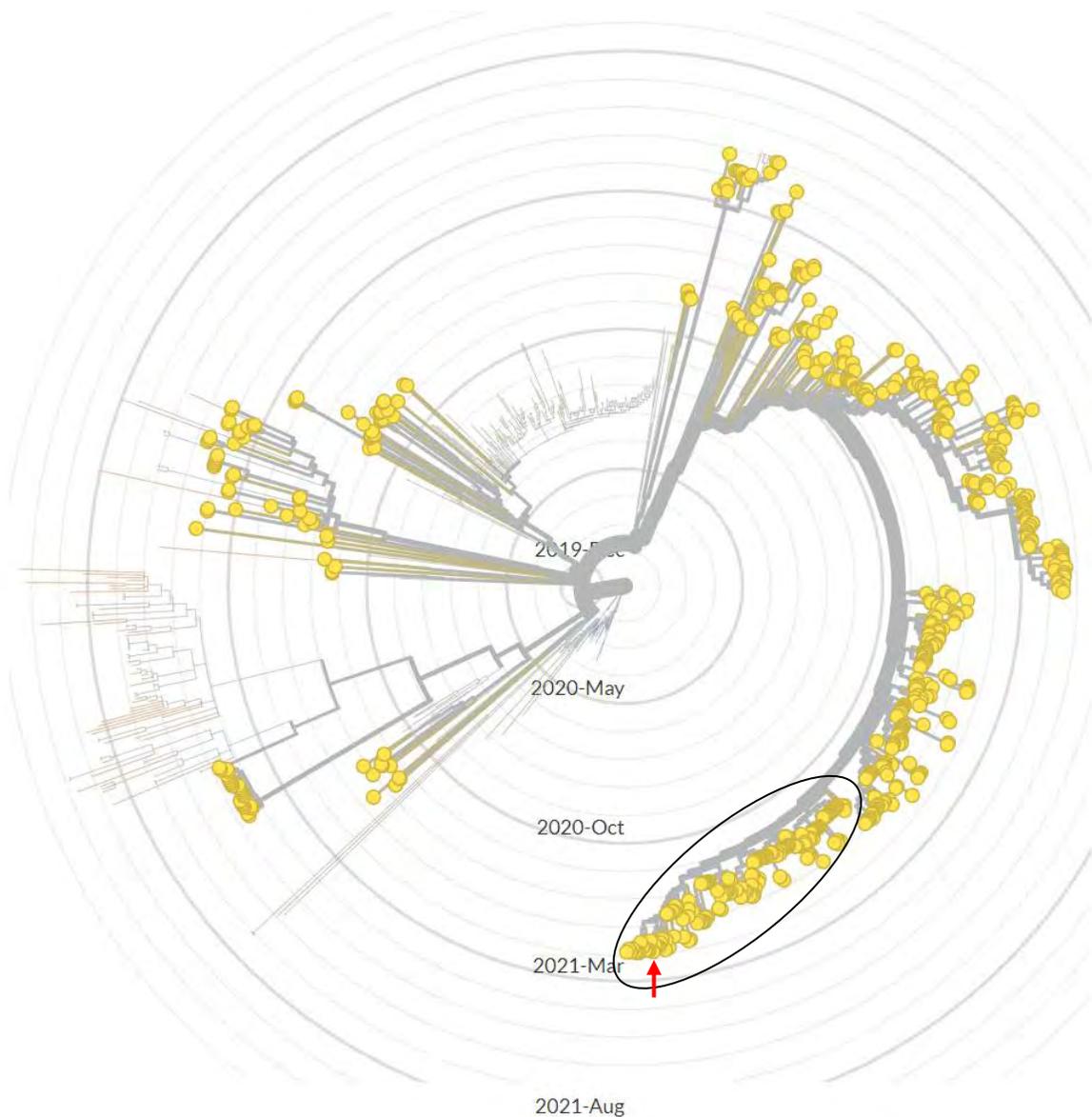


Transmission Chain 1

- Central Kowloon Tunnel
- K11 Musea
- Caritas Lok Yi School
- Ursus Fitness
- Sporadic cases (n=20) in Tuen Mun (in April 2021)

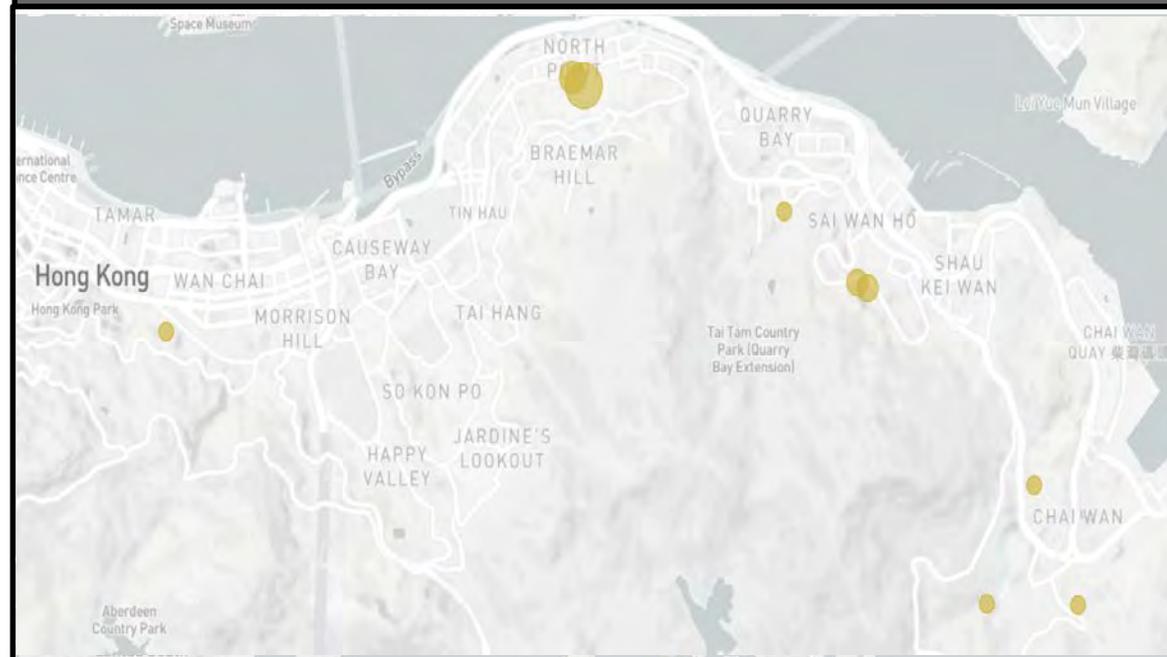


4th wave of outbreak (Nov 2020 – April 2021)

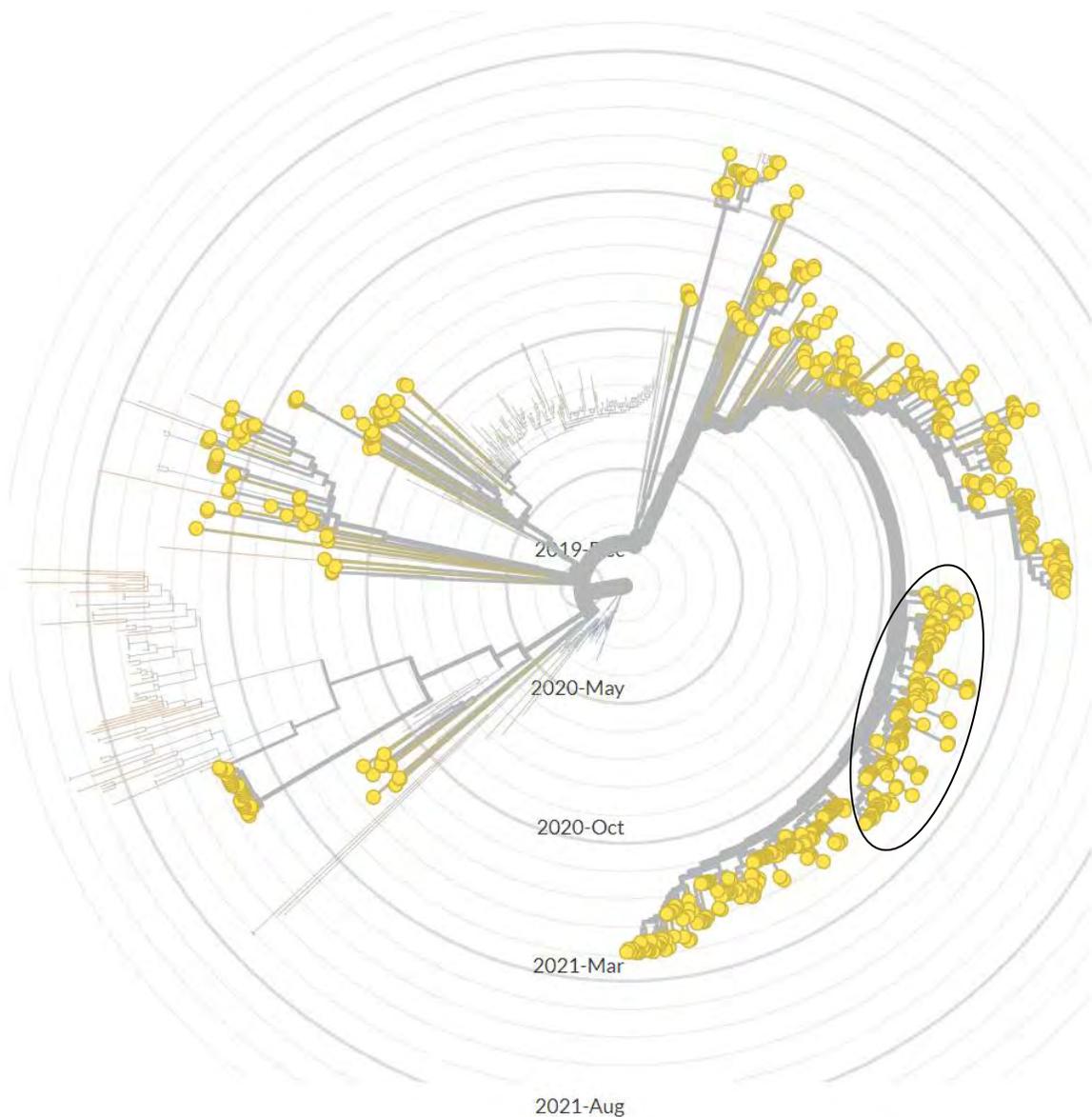


Transmission Chain 2

- Fong Shu Chuen Day Activity Centre
- LOHAS Park Construction site
- Artificial Island of HZM bridge
- Princess Margaret Hospital Medical Day Ward
- Sporadic cases (n=18) in Eastern District (Jan 2021)

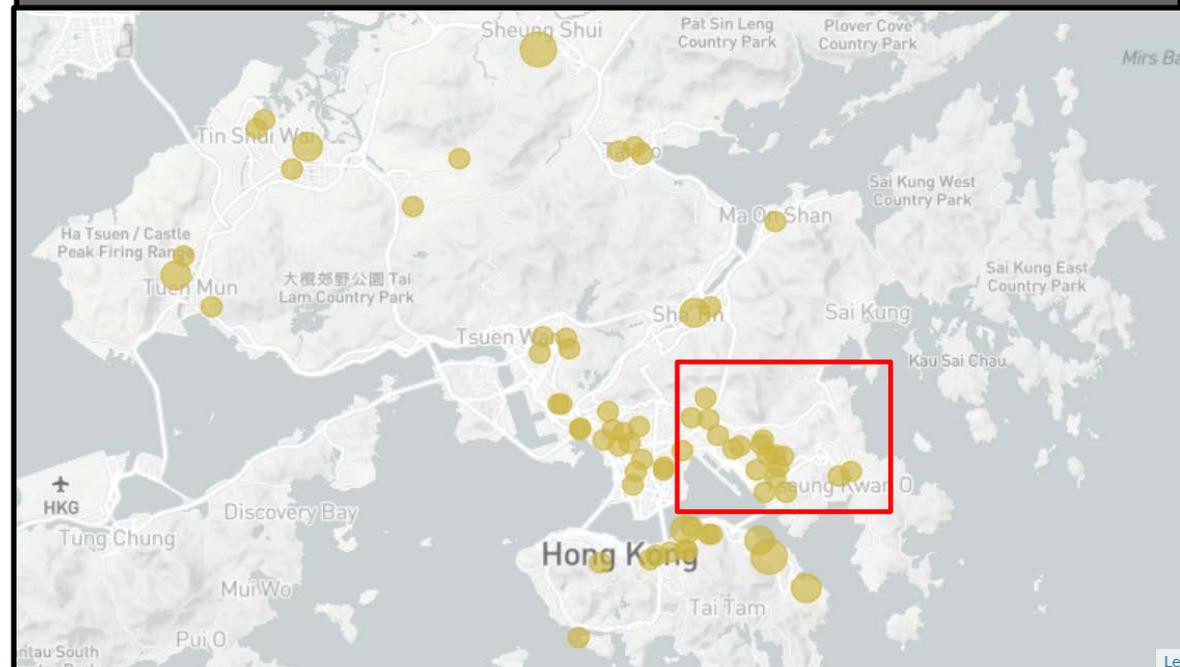


4th wave of outbreak (Nov 2020 – April 2021)



Transmission Chain 3

- Chuen Cheung Kui Restaurant
- Otto Mezza 8½ Bombana
- Sporadic cases in Kowloon East District
- United Christian Hospital Palliative and Medical



Phylogeographic Study of hospital outbreak

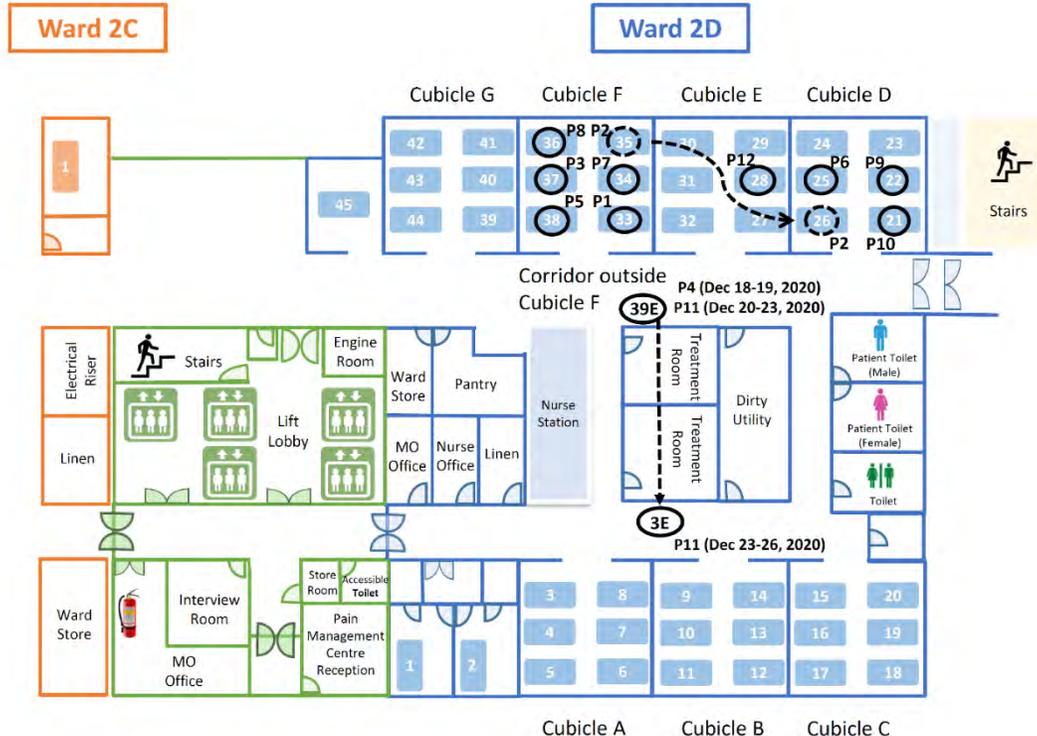
Clinical Infectious Diseases

MAJOR ARTICLE



Nosocomial Outbreak of Coronavirus Disease 2019 by Possible Airborne Transmission Leading to a Superspreading Event

Vincent Chi-Chung Cheng,^{1,2*} Kitty Sau-Chun Fung,^{3,4*} Gilman Kit-Hang Siu,^{4,5*} Shuk-Ching Wong,^{1,4*} Lily Shui-Kuen Cheng,³ Man-Sing Wong,⁵ Lam-Kwong Lee,⁶ Wan-Mui Chan,⁶ Ka-Yee Chau,³ Jake Siu-Lun Leung,⁴ Allen Wing-Ho Chu,⁶ Wai-Shan Chan,⁶ Kelvin Keru Lu,⁴ Kingsley King-Gee Tam,⁶ Jonathan Daniel Ip,⁶ Kenneth Siu-Sing Leung,⁶ David Christopher Lung,⁷ Herman Tse,⁸ Kelvin Kai-Wang To,⁹ and Kwok-Yung Yuen⁶



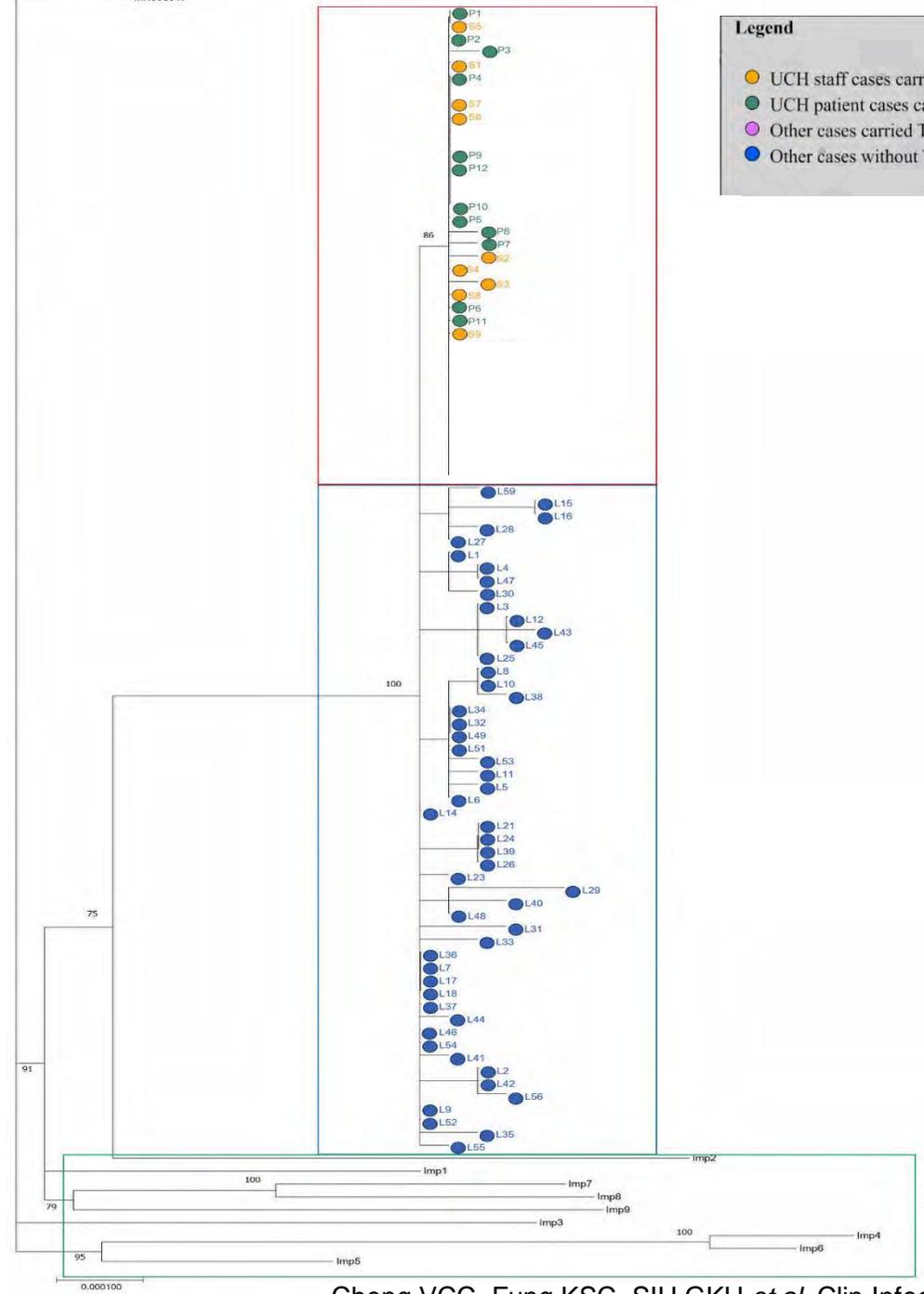
Period: 18 Dec – 30 Dec 2020

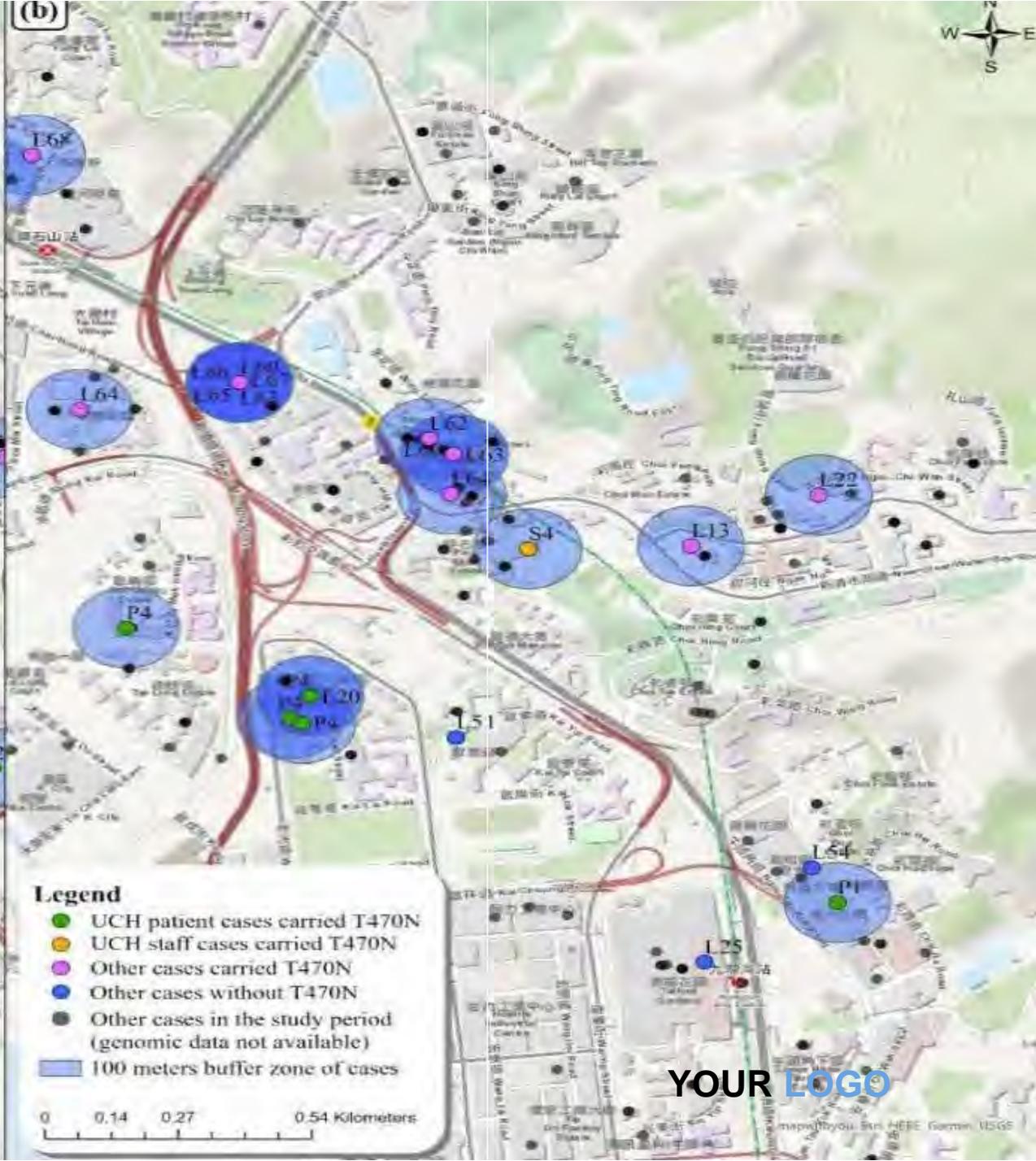
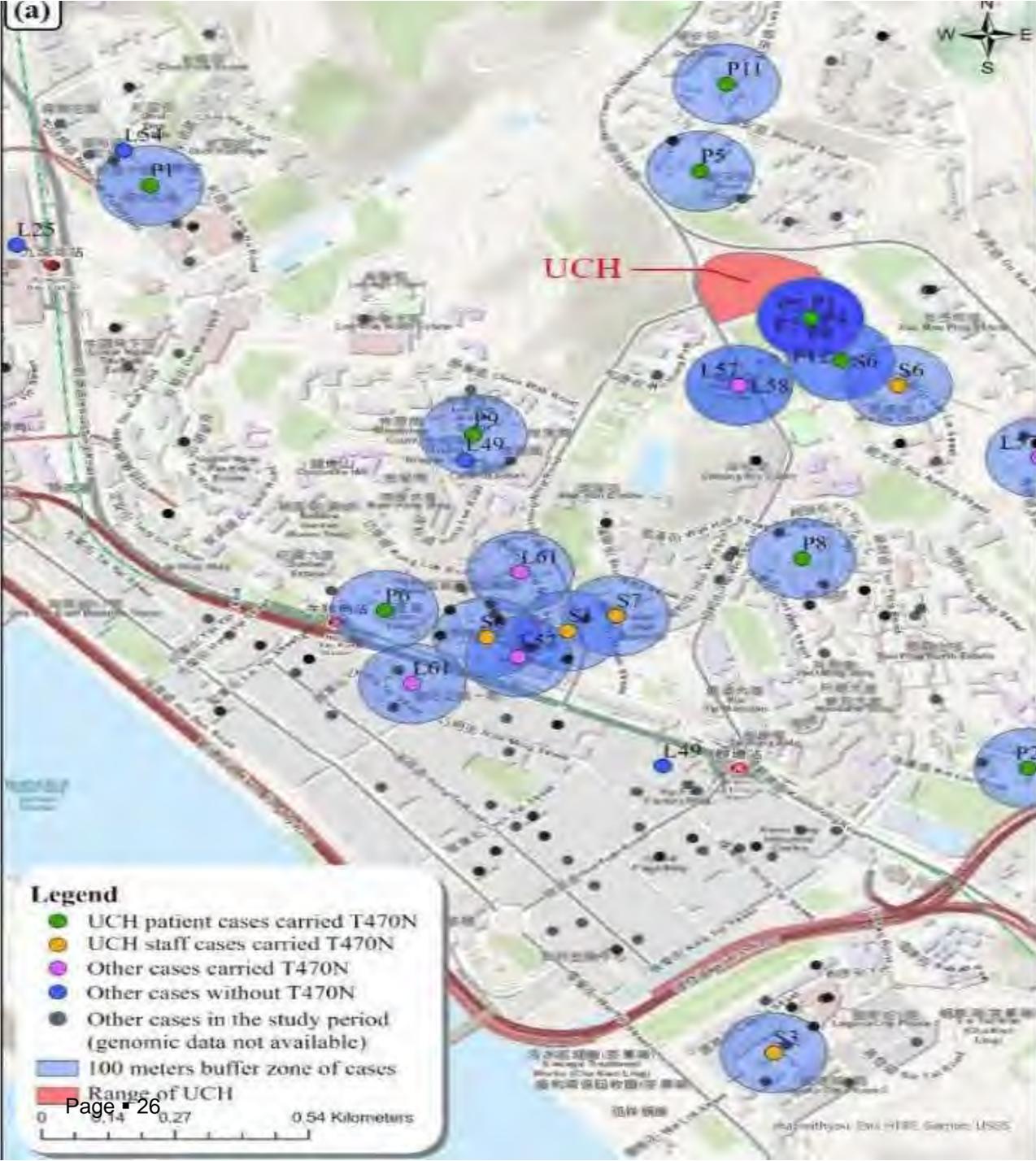
Location: General Medical & Palliative care ward

Case: 12 patients and 9 staff

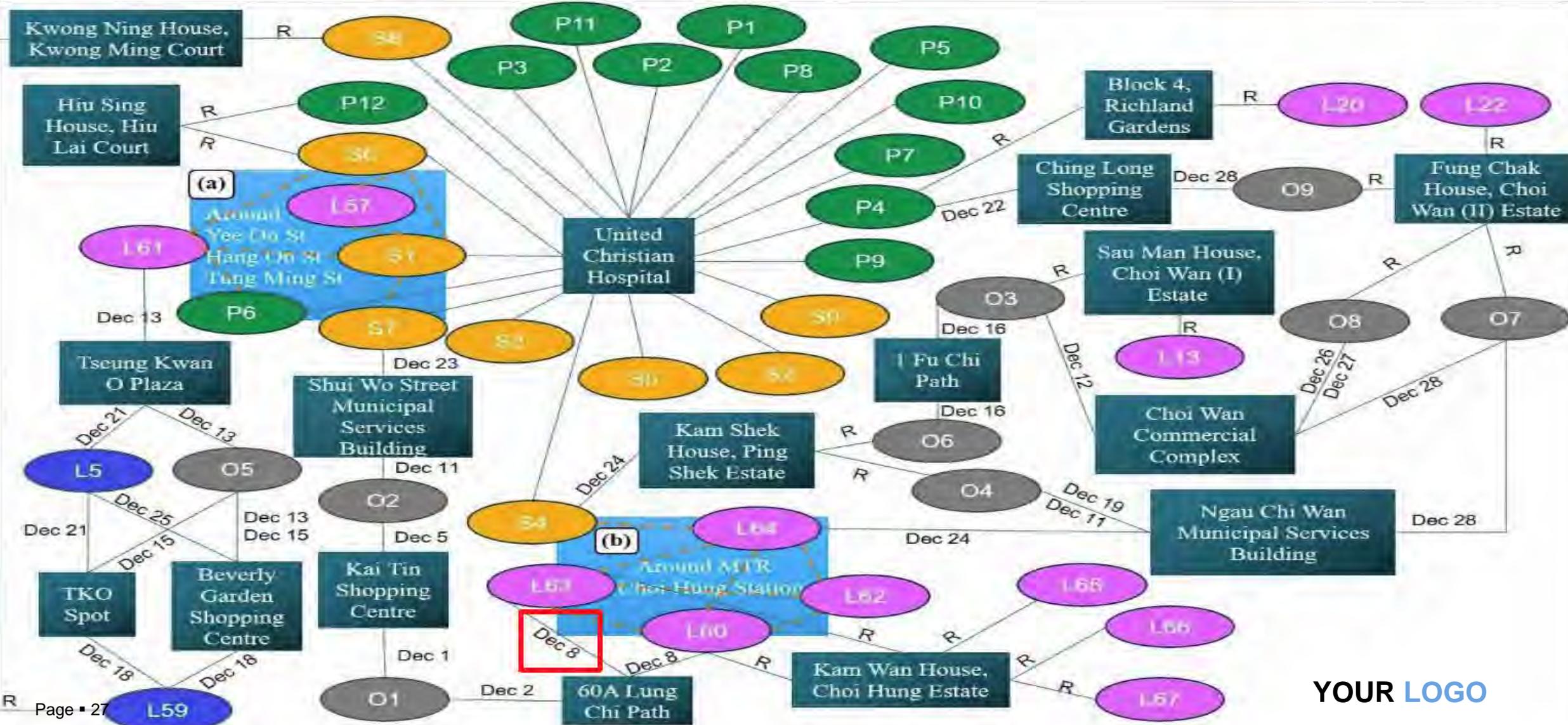
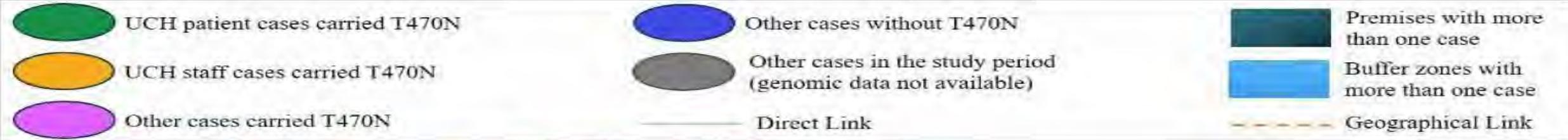
Legend

- UCH staff cases carried T470N
- UCH patient cases carried T470N
- Other cases carried T470N
- Other cases without T470N





YOUR LOGO



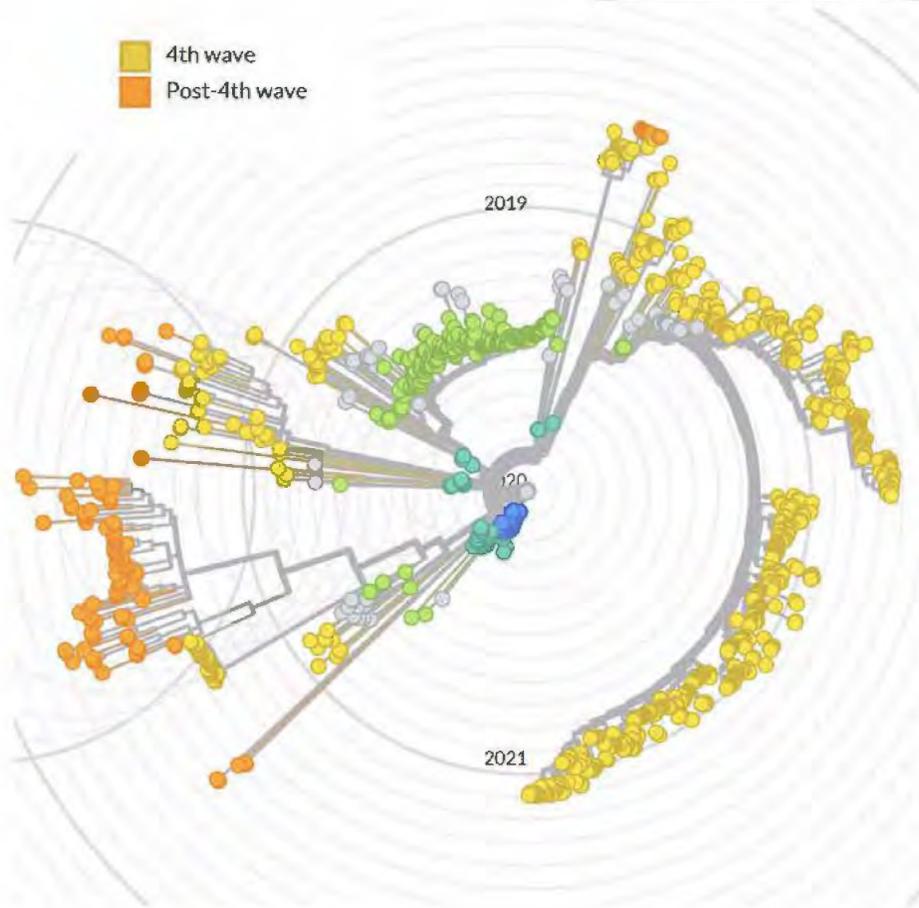
Beyond the 4th wave

Phylogeny

Wave ▾

- 1st wave
- 2nd wave
- 3rd wave

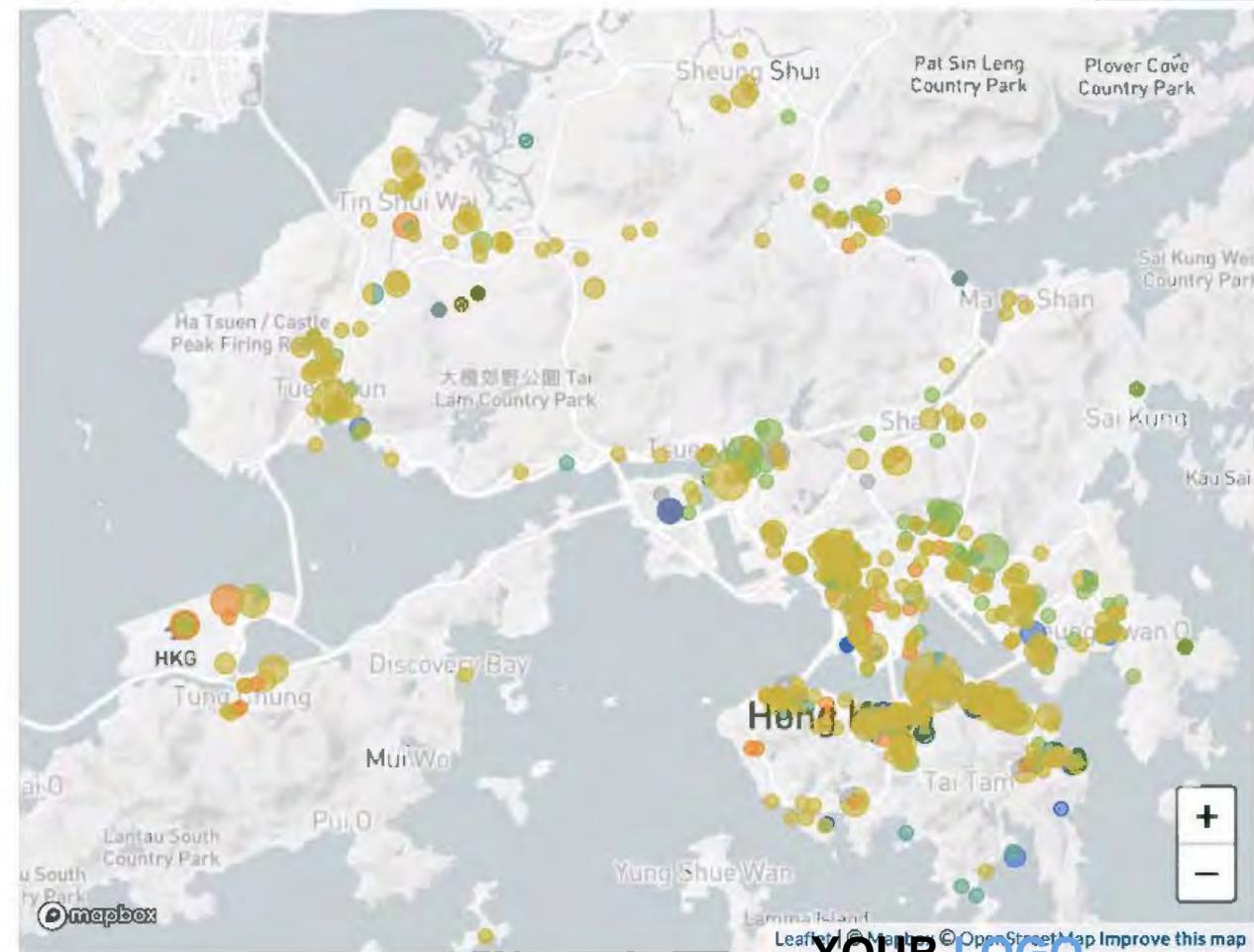
- 4th wave
- Post-4th wave



🔍 ZOOM TO SELECTED | RESET LAYOUT

Geography

RESET ZOOM



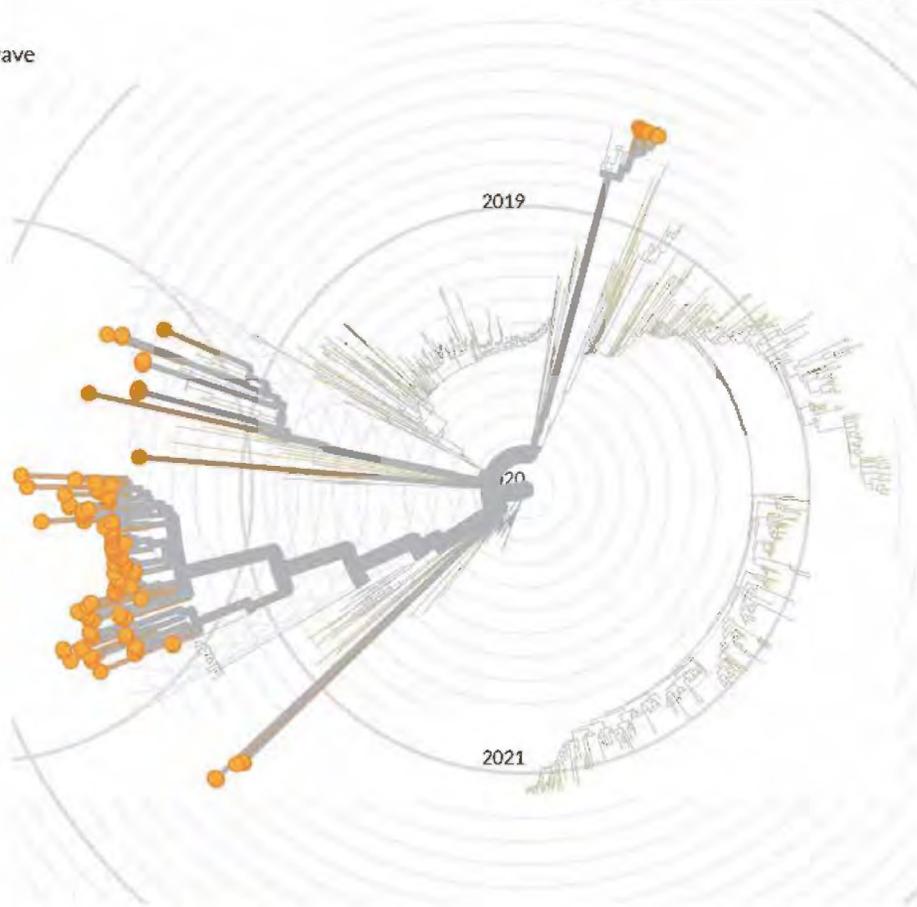
YOUR LOGO

Beyond the 4th wave

Phylogeny

Wave ▾

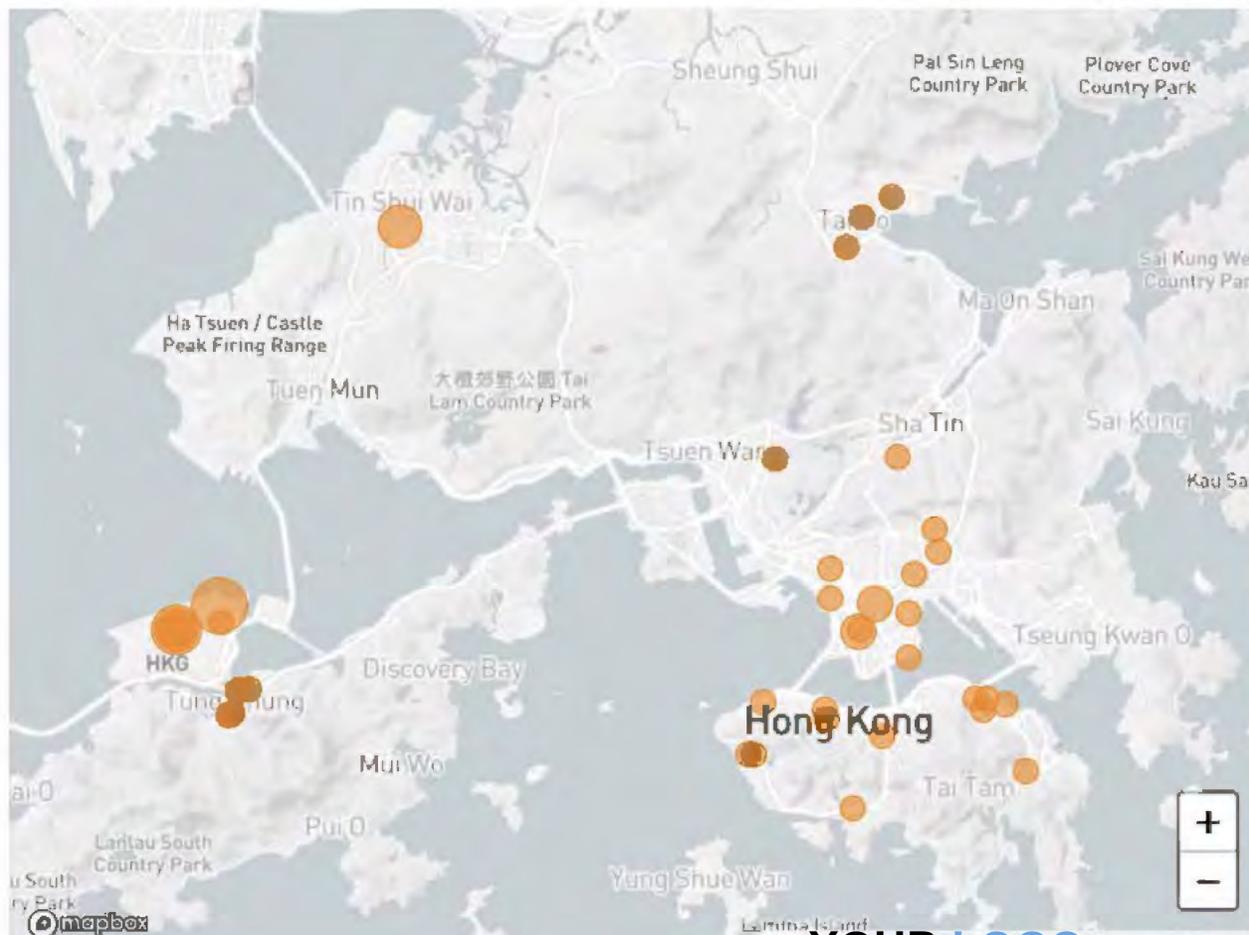
Post-4th wave



SEARCH ZOOM TO SELECTED RESET LAYOUT

Geography

RESET ZOOM



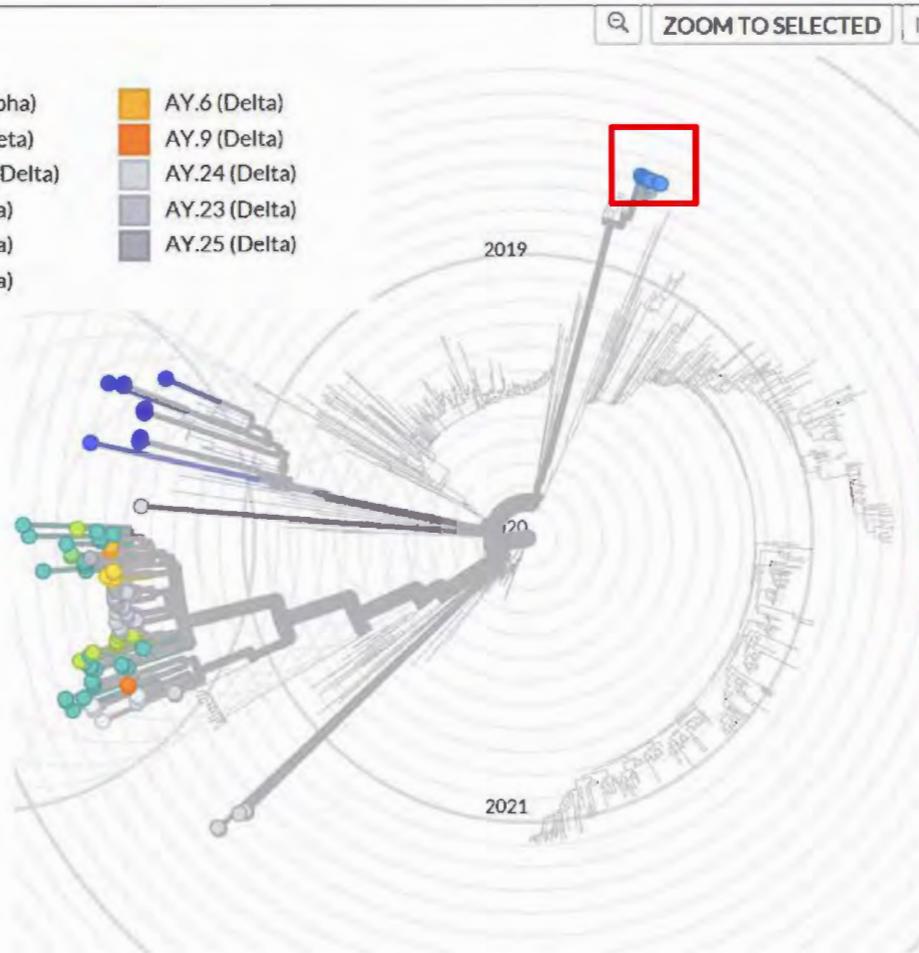
YOUR LOGO

Beyond the 4th wave

Phylogeny

VOC/VOV

- B.1.1.7 (Alpha)
- B.1.351 (Beta)
- B.1.617.2 (Delta)
- AY.3 (Delta)
- AY.4 (Delta)
- AY.5 (Delta)
- AY.6 (Delta)
- AY.9 (Delta)
- AY.24 (Delta)
- AY.23 (Delta)
- AY.25 (Delta)

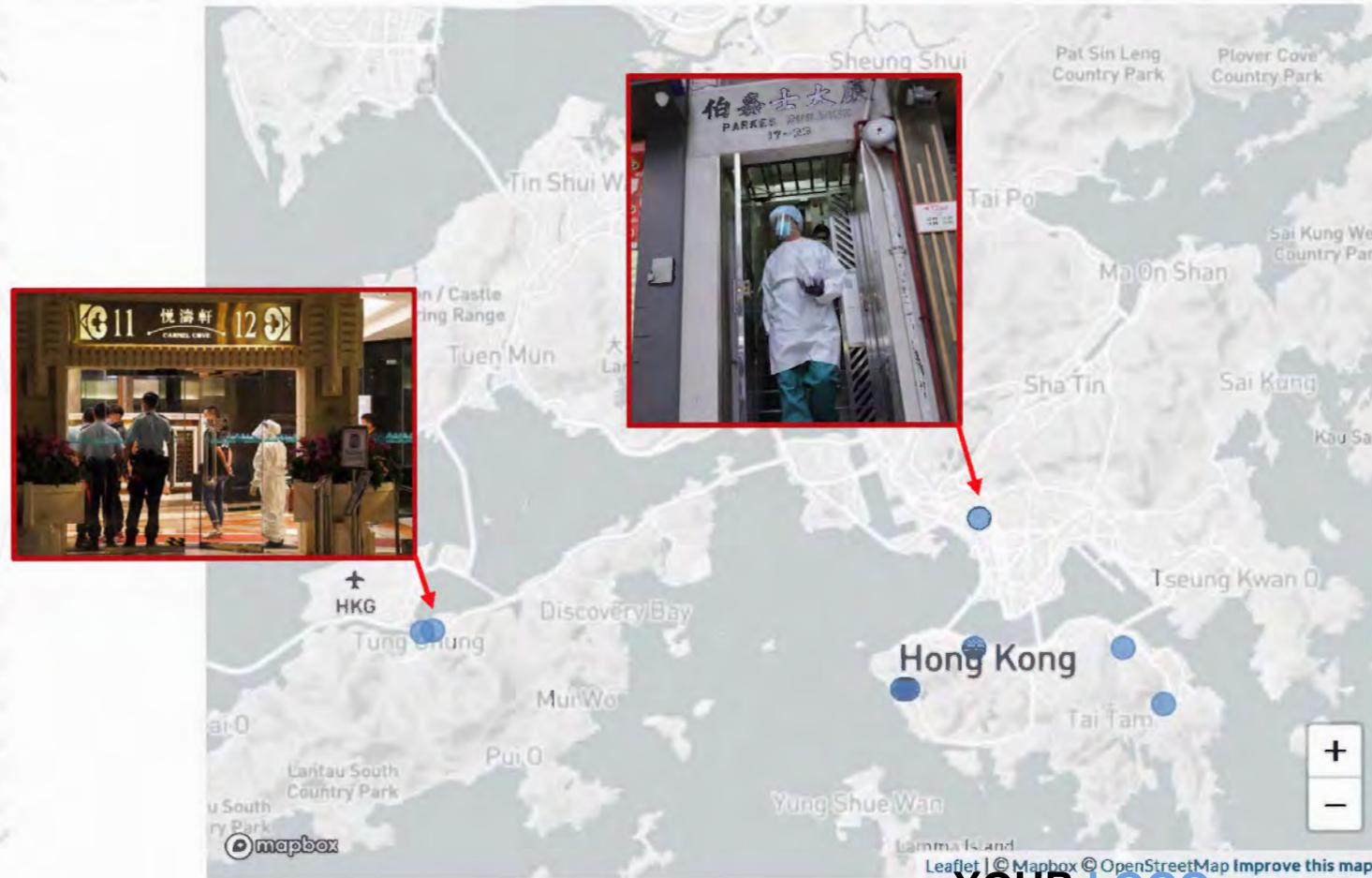


ZOOM TO SELECTED

RESET LAYOUT

Geography

RESET ZOOM



THE LANCET *Regional Health* Western Pacific

Complementation of contact tracing by mass testing for successful containment of beta COVID-19 variant (SARS-CoV-2 VOC B.1.351) epidemic in Hong Kong

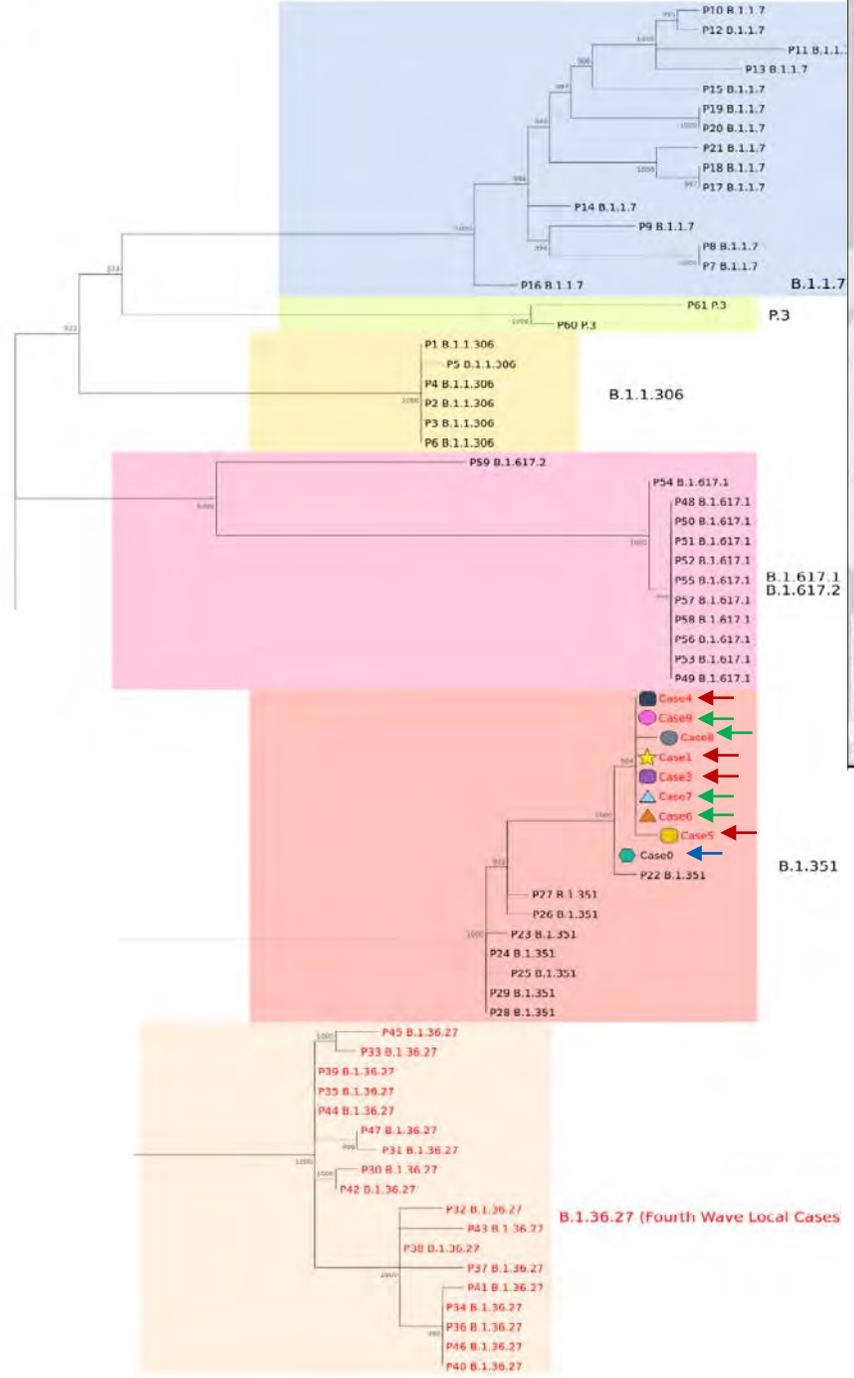
Vincent Chi-Chung Cheng^{*,1,2} Gilman Kit-Hang Siu^{*,3} Shuk-Ching Wong^{*,1} Albert Ka-Wing Au,⁴ Cecilia Suk-Fun Ng,⁴ Hong Chen,⁴ Xin Li,² Lam-Kwong Lee,³ Jake Siu-Lun Leung,³ Kelvin Keru Lu,³ Hazel Wing-Hei Lo,⁵ Evelyn Yin-Kwan Wong,³ Shik Luk,⁵ Bosco Hoi-Shiu Lam,⁵ Wing-Kin To,⁵ Rodney Allan Lee,⁶ David Christopher Lung,⁷ Mike Yat-Wah Kwan,⁸ Herman Tse,⁹ Shuk Kwan Chuang,⁴ Kelvin Kai-Wang To,¹⁰ Kwok-Yung Yuen¹⁰

8 Apr 2021
(D1) a



Tested positive on 17 and 18 Apr

(b)



(a)



Legend

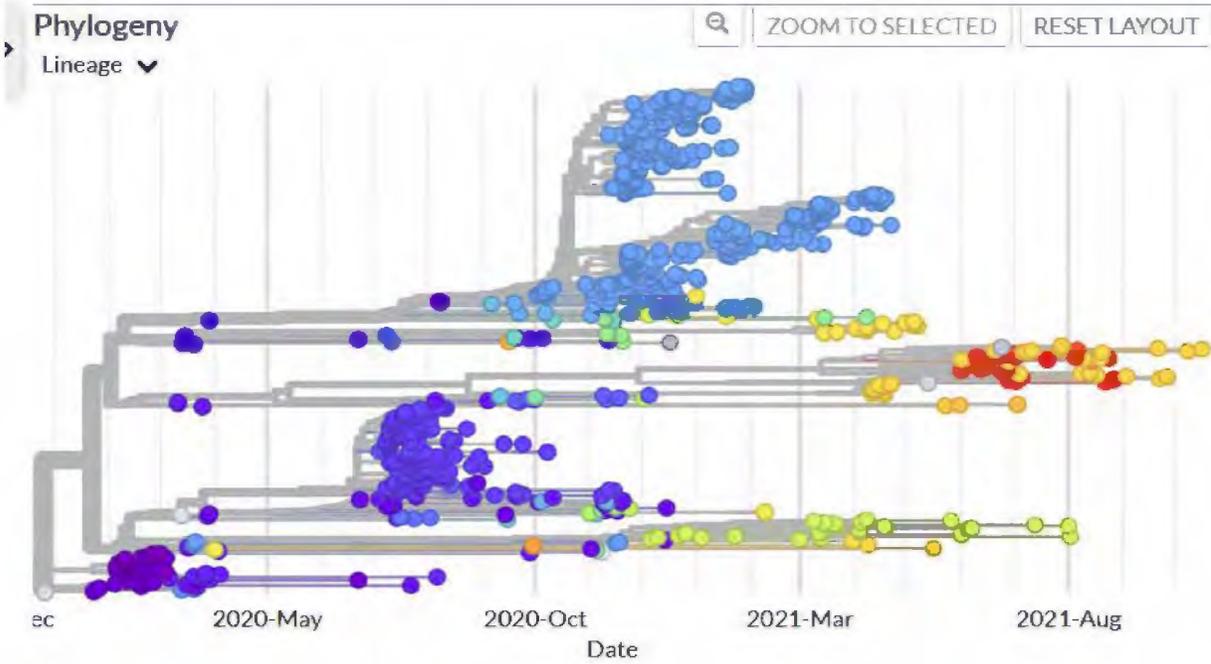
Index case: ⚡ Case 1

Family group one: ● Case 2 ● Case 8 ● Case 9 ● Case 10 ● Case 11

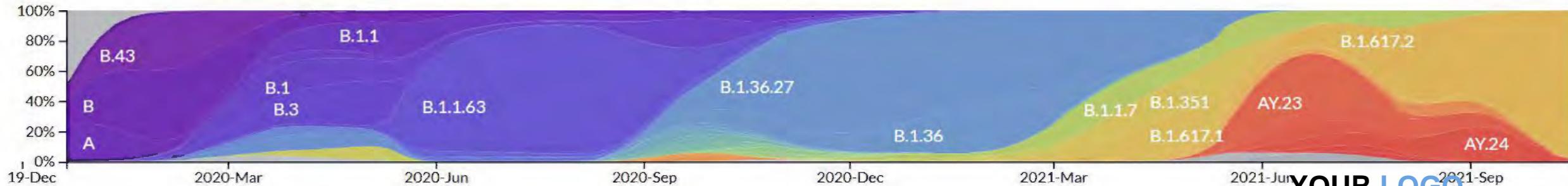
Family group two: ● Case 3 ● Case 4 ● Case 5

Other cases: ● Case 0 ▲ Case 6 ▲ Case 7

Geo-phylogenetic database for COVID-19 in Hong Kong



Frequencies (colored by Lineage)

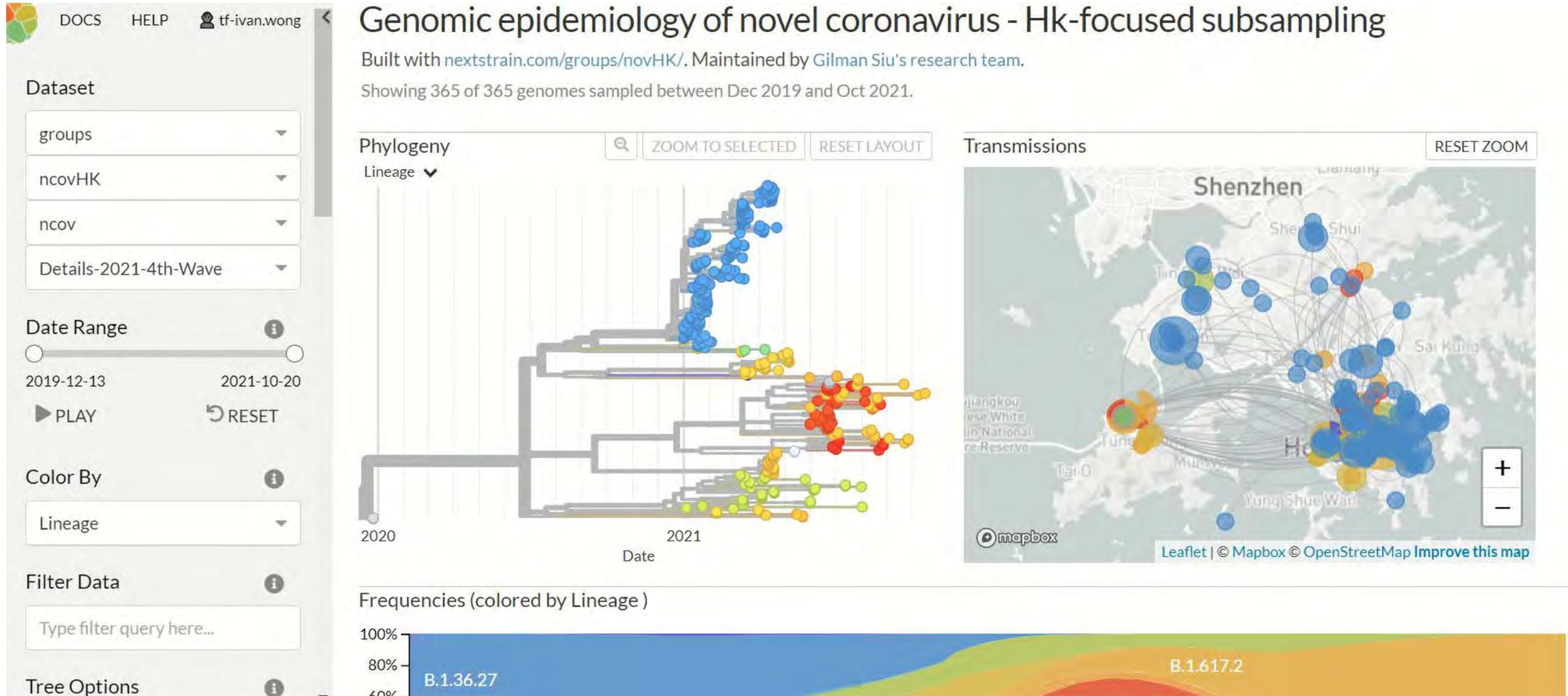


YOUR LOGO

<https://nextstrain.org/groups/ncovHK/ncov/Overview-2020Jan-2021Oct>

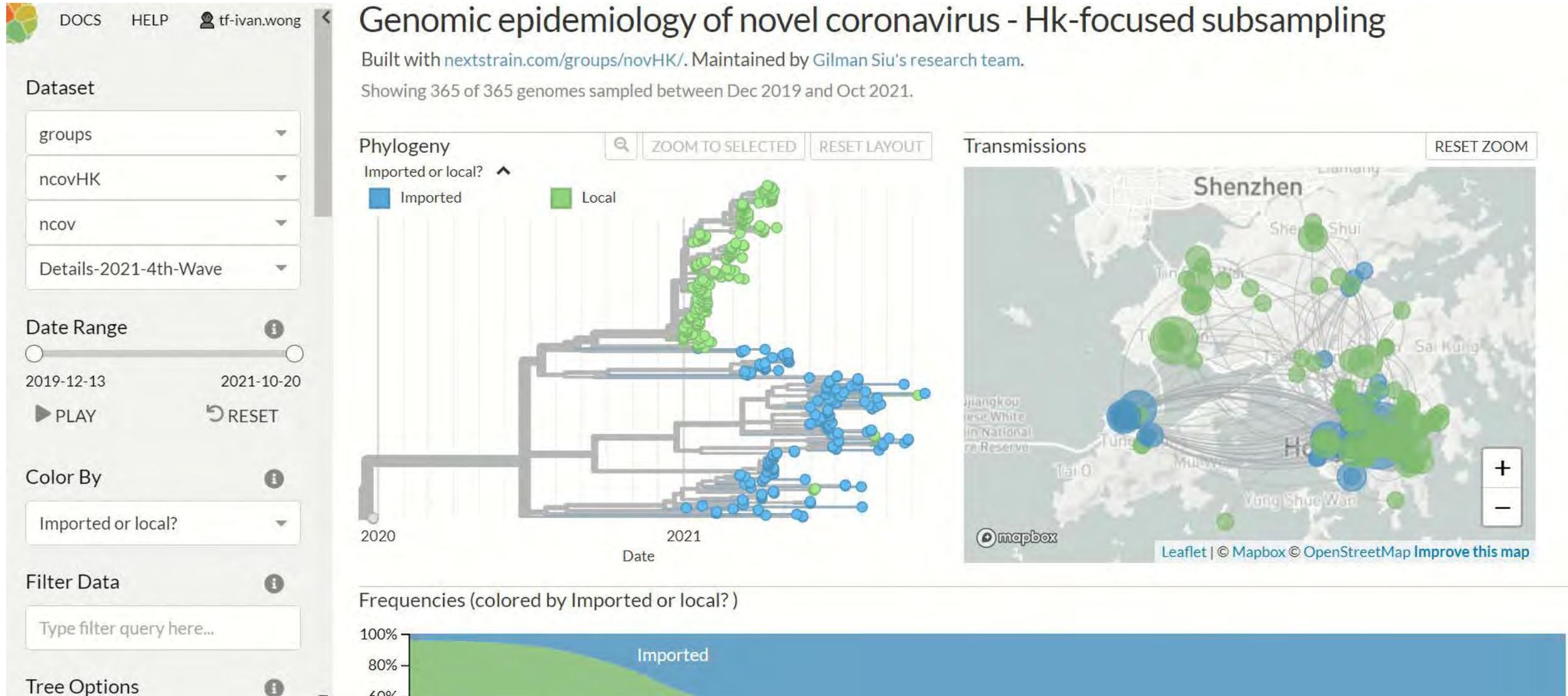
Geo-phylogenetic database for COVID-19 in Hong Kong

- Colour the cases with different attributes



Geo-phylogenetic database for COVID-19 in Hong Kong

- Filter out the cases with Delta variant Lineage AY.43



Geo-phylogenetic database for COVID-19 in Hong Kong

Filter out the cases in Tai Po

Date Range

2019-12-13 2021-

PLAY RESI

Color By

Lineage

Filter Data

Type filter query here...

Currently selected filter categories:

1 x Lineage

Tree Options

Layout

RECTANGULAR

RADIAL

UNROOTED

CLOCK

SCATTER

Hong Kong / Health & Environment

Coronavirus Hong Kong: city detects first suspected local case involving Delta variant; overnight lockdowns ordered in Tai Po

- As of Thursday morning, overnight testing had identified no positive cases at estate where coronavirus was detected in sewage samples
- If confirmed, the infection would end a 16-day streak of zero local cases



Victor Ting, Elizabeth Cheung and Danny Lee
Published: 1:55pm, 23 Jun, 2021

Why you can trust SCMP



Coronavirus - Hk-focused subsampling

Research team.

Filter to AY.23 (22)

Transmissions

RESET ZOOM



Point for 22 out of a total of 365 tips)

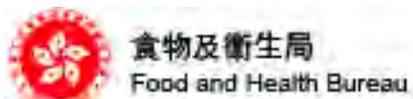
Take home messages

- **Geo-phylogenetic database for COVID-19 in Hong Kong, composed of > 1,000 SARS-CoV-2 genomes, is established**
- **Tree time and the interactive map can help to visualize the spatiotemporal spread of a viral strain in nearly real time**
- **If it is helpful, we are willing to disseminate the whole database and the soft code to CHP**
- **Wish to establish alliance with other institutions to enhance the coverage of genomic surveillance of SARS-CoV-2 in Hong Kong**

Acknowledgement



Funding supported by



HMRF commissioned project
COVID190204



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