17 May 2024

COVID-19 Genomics Insights (CGI) Report #48

CGID provides a public and high-level overview of SARS-CoV-2 genomic surveillance across Aotearoa New Zealand. It aims to explore and explain how whole genome sequencing (WGS) complements other epidemiological data to support public health decision-making. As SARS-CoV-2 continues to adapt and mutate, the CGI will highlight scientific research on viral evolution in New Zealand and overseas.

Summary Infographic & Insights:

genomes analysed

754

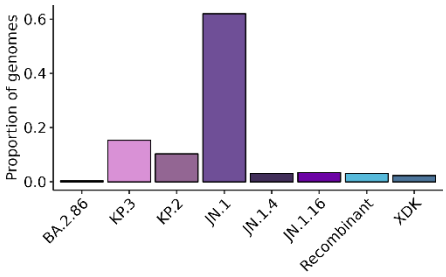
genomes from cases reported since the last CGI report (12 April 2024)

~4000

genomes* reported in 2024

variant & lineage

While JN.1 still represents more than half of sequenced cases, several JN.1-derived variants are starting to emerge, such as KP.3 (16%), KP.2 (11%) and JN.1.16 (4%)



hospital cases

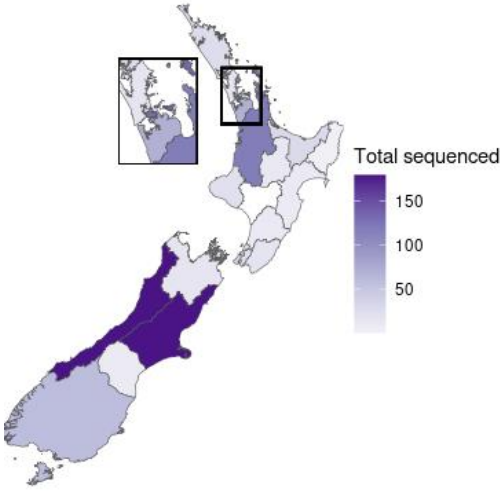
36% (67 of 187*) of PCR-positive cases with a hospital admission date from 20 April to 10 May have been sequenced to date.

The approximate composition of hospital cases:

- JN.1 68%
- JN.1.16 3%
- KP.3 13%
- KP.2 7%
- Recombinant 5%
- JN.1.4 3%

*The total number of PCR positive admitted cases includes high Ct samples not suitable for sequencing, samples that fail to produce genomes and cases reported late in the reporting period.

Origin of sequenced samples



Number of SARS-CoV-2 genomes sequenced

Key trends and insights

- 99.6% of genomes from cases reported in the last two weeks descend from JN.1 (with only BA.2.86, the ancestor of JN.1, also detected).
- Different JN.1 lineages have converged on a set of mutations in the spike protein associated with increased transmissibility, including two changes collectively referred to as the “FLiRT” mutations.
- KP.3 (a lineage containing one of the FLIRT mutations) and KP.2 (which contains both) are growing in frequency. LB.1, a lineage with both FLiRT mutations has been identified as an emerging lineage to watch closely.
- The latest wastewater results mirror those from whole genome sequencing from clinicals, with the appearance of JN.1 sub-lineages.

WGS sampling

ESR continues to request PCR-positive samples with PCR Ct values less than 30 (and samples with no recorded Ct) from cases not recently sequenced. Since the last CGI report, 754 genomes have been added to the WGS surveillance dataset. Sequenced cases are not a random or representative sample. The most notable bias is in the age of sequenced cases, with older and younger cases overrepresented in sequencing (**Figure 1**).

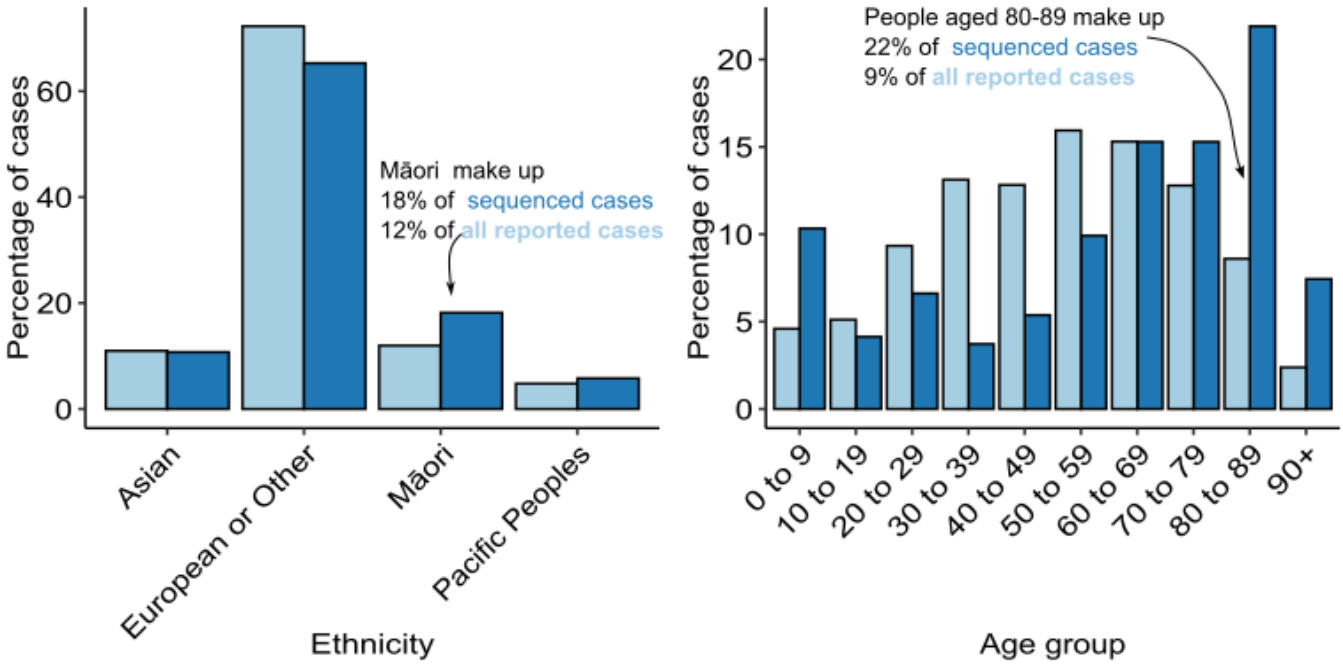


Figure 1. Left: *Distribution of sequenced cases (dark blue) and all reported cases (light blue) by ethnicity. Each case is assigned to a single ethnicity for this analysis, with priority order Māori, Pacific Peoples, Asian, European or Other.* ***Right****: Distribution of reported and sequenced cases by age.*

Tracked Variants

Tracking the frequency and epidemiological properties of SARS-CoV-2 variants is a key goal of the CGID. These reports follow the Pango nomenclature to classify sequences (https://cov-lineages.org/). The specific lineages of the sequenced genomes are then grouped into higher-level classifications representing the evolutionary relationships between lineages. **Figure 2** describes the set of tracked variants used for this report and how they relate to each other.

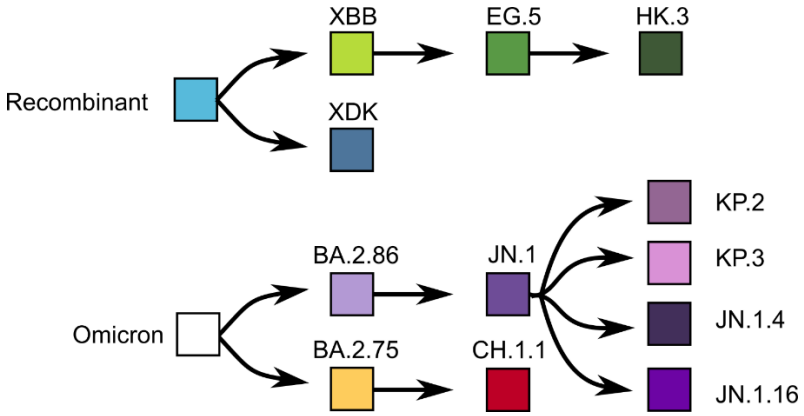


***Figure** 2. Relationships between the variants tracked in this report.*

Overview of sequenced cases

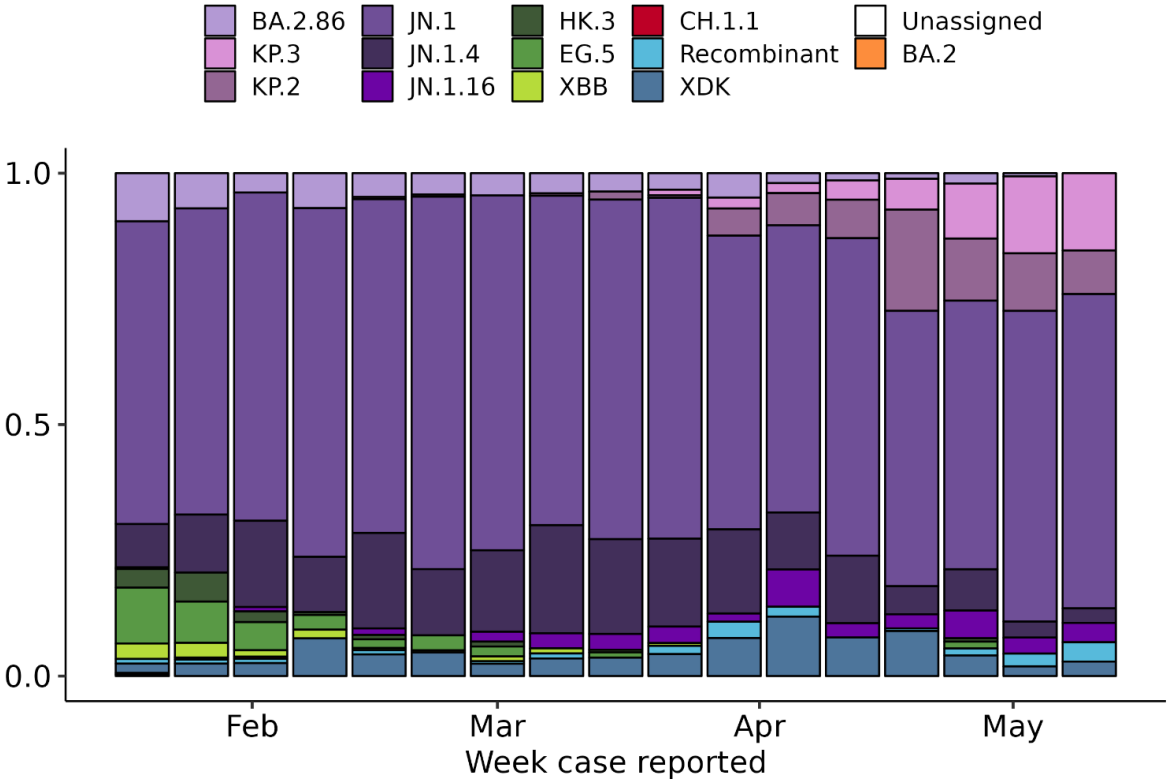


***Figure** 3. Frequency of variants/lineages in the past 17 weeks. Note, data for the most recent two weeks is preliminary. It will be updated as additional cases reported within these weeks are referred to ESR and sequenced. Data from the last reporting week is based on 104 genomes. Tracked lineages are defined in **Figure 2**.*

JN.1 sub-lineages converge on advantageous mutations.

Several of the JN.1 sub-lineages identified as “emerging lineages” in the last report have continued to grow over April and the first weeks of May and now make a substantial proportion of sequenced genomes. The sub-lineages KP.2 (11% of sequenced cases reported in the last two weeks), KP.3 (15%) JN.1.16 (4%) have all been added to the tracked lineages. These sub-lineages have each acquired at least one of two key mutations in the spike protein, labelled R346T and F456L, which are sometimes collectively labelled as the “FLiRT” mutations (**Figure 4**).

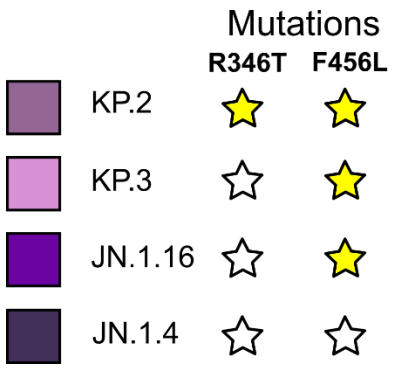


Figure 4. *Distribution of the key FLiRT mutations among tracked JN.1 variants.*

Emerging Lineages

ESR analyses SARS-CoV-2 genomic surveillance data closely to identify any emerging lineages that may have a growth advantage over the currently dominant JN.1 (**Figure 5**). For this report, three lineages currently reported under JN.1 have been singled out for closer examination. **The most interesting of these is LB.1** This lineage contains both of the FLiRT mutations as well as another spike mutation (a deletion in position 31). This lineage was first detected in New Zealand in a case reported in April and has grown to 6% of sequenced cases reported in the last two weeks. ESR will monitor the growth of LB.1 and other lineages in the coming weeks.

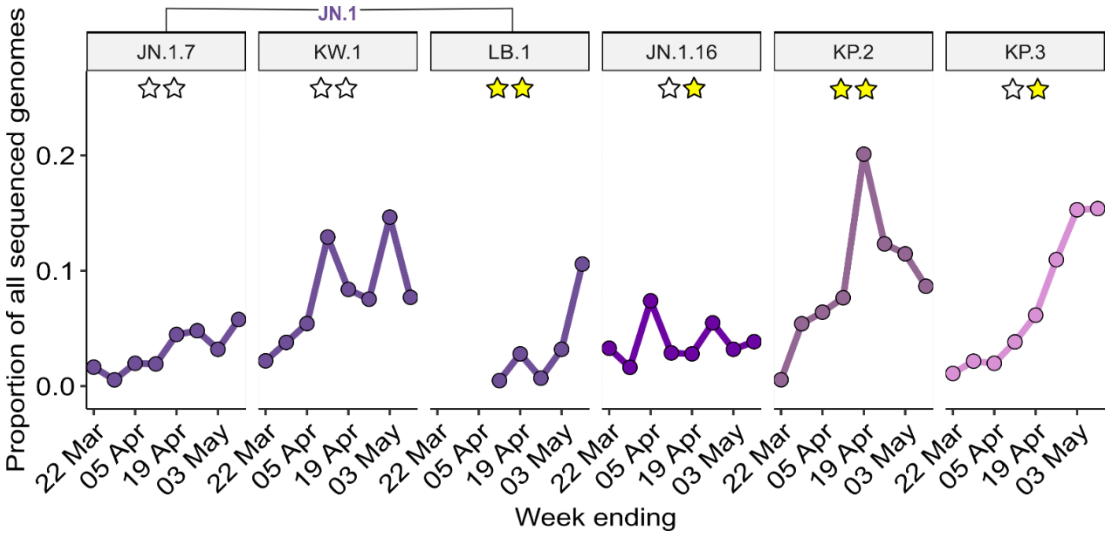


Figure 5. *Frequency of specific lineages in recent weeks. Each sub-plot represents data from a single lineage, and all its descendant lineages not included elsewhere in this graph. The yellow stars above each plot represent the presence of one or both “FLiRT” mutations (see below) in each genome. The leftmost three lineages are currently reported within the JN.1 lineage classification*

Tracking Specific Mutations

The growth of lineages such as LB.1, KP.2 and KP.3 is part of a wider trend in which key mutations in the spike protein have been observed to provide growth advantages in multiple different JN.1 lineages. As different JN.1 lineages converge on the same set of advantageous mutations, we have begun to track the frequency of these mutations independently of the specific lineages carrying them.

For this report we have designated the two FLiRT mutations (R346T and F456L) as well as the deletion found in LB.1 and a substitution labelled T572I as key mutations for tracking. The proportion of sequenced genomes containing any number of these four key mutations has risen steadily in recent weeks, with 36% of genomes from cases reported in the last two weeks containing two or more of these changes (**Figure 6**). No genomes with all four mutations have been detected in New Zealand to date. ESR will continue to monitor these mutations closely and, if appropriate, provide growth advantage estimates associated with combinations of mutations regardless of their genomic lineage.

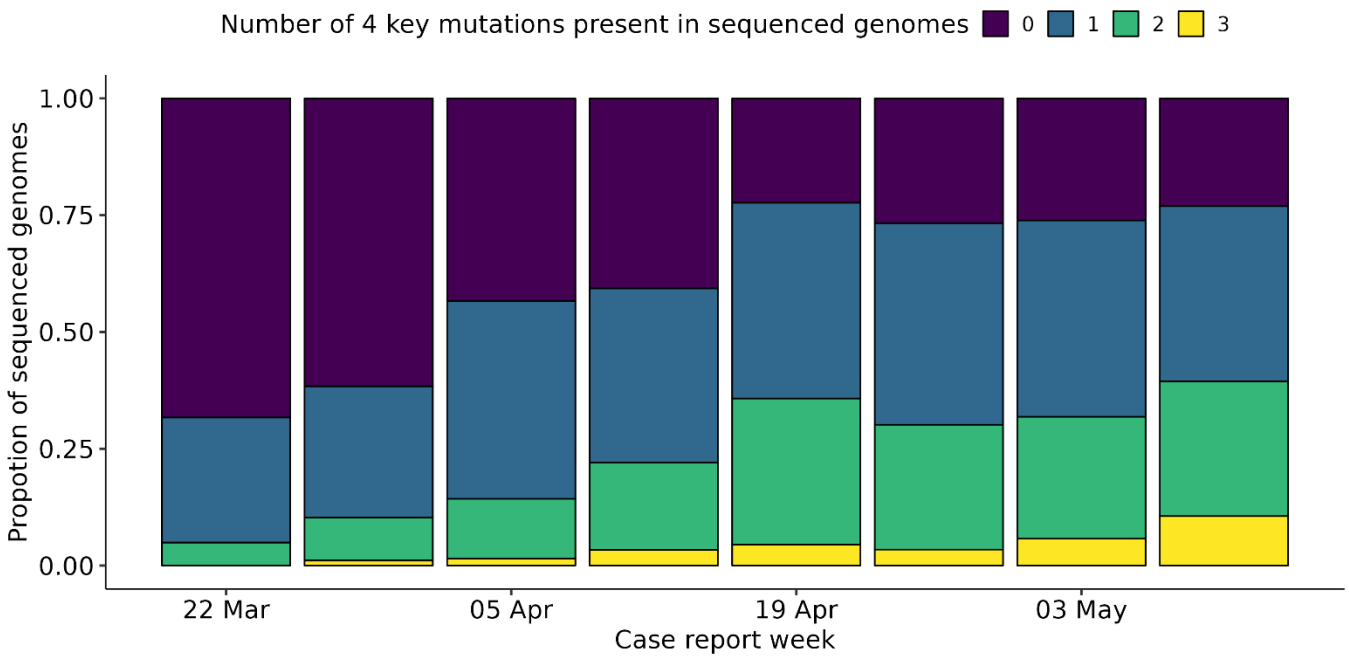


Figure 6. *Frequency of genomes containing between zero and 4 of a set of specific spike protein mutations (R346T, F456L T572I and S31Del) potentially associated with increased transmissibility.*