COG UK
COVID-19 GENOMICS UK CONSORTIUM

Summary report of COVID-19 reinfection

Prepared on behalf of COG-UK by:
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Report on the SARS-CoV-2 genomic analysis presented in:

Kai-Wang To *et al.* (2020) "COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing" *Clinical Infectious Diseases*, https://doi.org/10.1093/cid/ciaa1275

Summary

This paper reports an apparent case of reinfection by a different SARS-CoV-2 variant 20 weeks after an initial confirmed infection. The individual is a 33 year old male Hong Kong resident.

First infection:

Confirmed 2020-03-26 by RT-PCR (mild symptom onset 3 days prior to this?).
Hospitalised 2020-03-29 (symptoms subsided).
Discharged 2020-04-14 after two negative RT-PCR tests.
Serum sample 10 days after symptom onset tested negative for IgG against SARS-CoV-2

Second infection:

Returned to Hong Kong from Spain via UK on 2020-08-15, positive RT-PCR test at airport.
Hospitalised but asymptomatic.
Increasing Ct in days post hospitalization suggests peak viral load was prior to arrival.
Serum sample on day 5 tested IgG positive (days 1-3 negative)

SARS-CoV-2 Genome analysis

Genome from March sample was in lineage B.2 and phylogenetically it groups with viruses from the UK and USA from this time period.

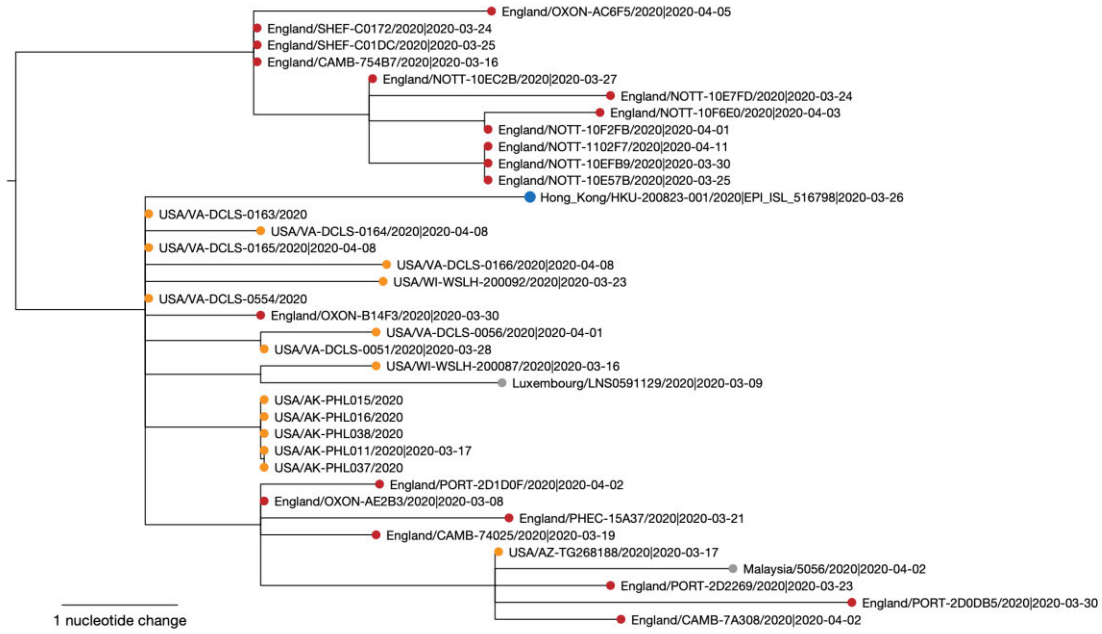

Figure 1 | Phylogenetic tree of the first episode genome (GISAID accession EPI_ISL_516798) and closely related genomes from lineage B.2. Dates of sample collection are appended to the end of genome labels where available.

Genome from August sample was in lineage B.1.79, a predominantly UK lineage (https://cov-lineages.org/lineages/lineage_B.1.79.html) which is compatible with the known travel history for the second episode. This most likely means that the individual acquired the second infection in the UK but the paper does not elaborate on the amount of time spent in the UK. It is unknown if B.1.79 is circulating in Spain but if so then likely it would have been imported from the UK at an earlier date.

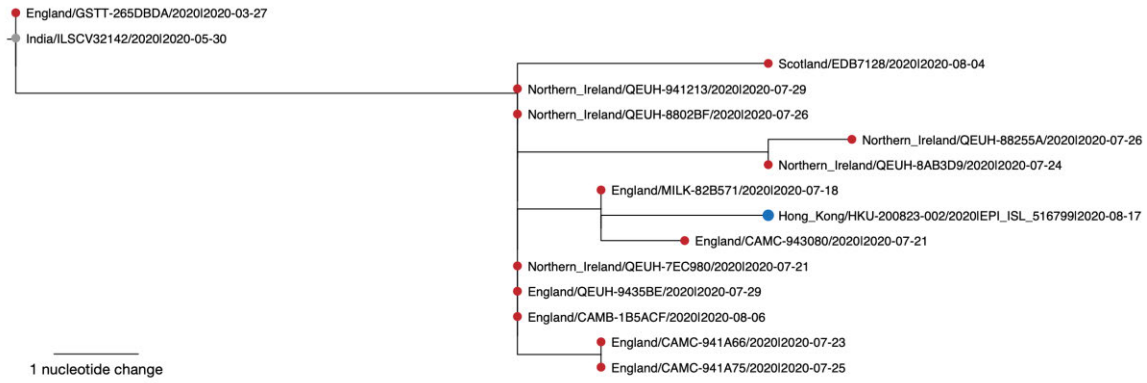

Figure 2 | Phylogenetic tree of the second episode genome (GISAID accession EPI_ISL_516799) and closely related genomes from lineage B.1.79. Dates of sample collection are appended to the end of genome labels where available.

Observations

The two genomes are genetically distinct and each cluster with genomes from around the respective time period that they were sampled.

The March genome has a mutation in the ORF8 gene which produces a stop codon resulting in a product that will be truncated by 58 amino acids. It is unknown what effect this will have on the protein's function but other large-scale mutations and deletions have been observed in ORF8 suggesting there may be little fitness cost to losing function.

The August genome contains the notable Spike mutation D614G however this is now the predominant variant globally so nothing should be inferred from this single instance.

Although asymptomatic, the later genome would not have been circulating in March so it is not the cause of the earlier infection (nor was it part of a coinfection then). If the earlier infection was a false positive then it would have to have been the result of a sample mix-up or contamination with other samples from that time.

Implications for the UK

Based on knowledge of other Coronaviruses, reinfection is to be expected, although at present the point at which an individual is likely to be susceptible to reinfection is not known. In cases that have begun to be reported, the time to reinfection in an individual has been relatively short. Where this is the case, genomics is required to demonstrate that the virus from the two infections is not the same, providing evidence to rule out recrudescence.

Large-scale genomic surveillance of positive samples from the UK may provide a data source that could identify potential reinfections, and the integration of key metadata could enable this to be done in an automated way. However, this will be dependent upon ensuring the appropriate data flows are available and ensuring that individuals are being tested for COVID-19 even when they have already had an infection which has resolved. Therefore, this may require public understanding that once they have had COVID-19 they can be reinfected, and should seek to be tested again if they present relevant symptoms.

If, as in the case of the individual in Hong Kong, reinfected individuals are asymptomatic, then it is imperative that work is undertaken - including a genomics component - to identify if these asymptomatic individuals are likely to be infectious. Clearly, if reinfections are both asymptomatic and infectious, this could pose challenges for any symptoms-based measures (e.g. requesting a test, self-isolating) used to try and limit/control the pandemic.

Ongoing genomics investigation of reinfection in the UK

Surveillance and monitoring in England

PHE is undertaking work to identify and investigate reinfections in the England.

SIREN is a prospective cohort study to determine the incidence of reinfection using a large cohort of seropositive and seronegative healthcare workers in the NHS.

Surveillance through the Second Generation Surveillance System: PHE undertakes routine monitoring of diagnostic laboratory data in England to identify individuals with two or more positive SARS-COV-2 RNA tests. Those with positive results detected more than 60 days apart are investigated and will be considered for further laboratory testing, including sequencing, where appropriate.

Potential reinfection cases identified through SIREN, surveillance, or by clinical referral to PHE are investigated and, if appropriate, sequenced under an arrangement with COG-UK. Genomic analysis is undertaken by PHE in conjunction with other available clinical and virological data.

PHE will report directly on reinfections if confirmed and additional data will be available through the SIREN interval analyses.

Surveillance and monitoring in Wales

Public Health Wales undetakes genomic-based surveillance of COVID-19 cases in Wales as part of the wider Surveillance Strategy for COVID-19, and is a constituent member of COG-UK. PHW has been successfully sequencing approximately 40% of all positive cases in Wales and the Pathogen Genomics team within PHW is performing active analyses on any patients who have multiple positive results spanning a time period of more than 28 days which have been sequenced successfully. No reinfections have been identified from this analysis to date.

In addition, the surveillance team within the Communicable Disease Surveillance Centre and the Specialised Virology Centre within PHW are actively tracking individuals with multiple positive SARS-CoV-2 test results. This surveillance has the option to request genome sequencing as well as to undertake further investigation as required.

One key issue for PHW is the sequencing of samples that are sent to lighthouse labs, and subsequent data linkage, as this covers an increasing number of community and self-test samples from Welsh patients. This issue is currently being addressed, through engagement via COG and engagement with DHSC by Welsh Government directly. It is likely that community samples/self-sampling will be particularly important for examining the question of reinfections going forward.

PHW is also involved in a number of antibody studies being undertaken in Wales, and since March has been performing a considerable number of diagnostic tests on healthcare workers, which have largely either been sequenced or are stored and could be re-extracted and sequenced. Where studies being undertaken in Wales identify potential reinfections, genomic analysis can be requested, and samples will be sequenced by the Pathogen Genomics Unit, with the results analysed by the PHW Bioinformatics team.