**Supplementary Table 1.** Temporal evolution of sample diversity and pairwise dissimilarities. The distributions support high significance of 0-1 variant difference between samples.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Number of samples | Median number of variants (AF≥0.5) per sample | Pairwise distance Mean | Pairwise distance SD | Percentage of pairs with distance≤1 | Distance≤1 p-value |
| Apr 2020 – Aug 2020 | 582 | 12 | 14.41 | 6.01 | 0.26% | 0.01283 |
| Sep 2020 - Nov 2020 | 488 | 16 | 22.86 | 6.28 | 0.17% | 0.00025 |
| Dec 2020 - Jan 2021 | 626 | 22 | 29.64 | 9.31 | 0.11% | 0.00105 |
| Combined | 1696 | 16 | 23.47 | 8.34 | 0.07% | 0.00355 |

**Supplementary Table 2.** Suspected clusters of viral transmission.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Sample # | Test Date | Patient or Staff | Cluster # | Unit # | Genomic Interpretation |
| 1 | 6/23/2020 | Patient | 1 | A | Highly related |
| 2 | 6/23/2020 | Staff  | 1 | A |
| 3 | 6/23/2020 | Staff  | 1 | A |
| 4 | 6/24/2020 | Staff  | 1 | A |
| 5 | 7/2/2020 | Parent | 1 | A | Low coverage |
| 6 | 7/1/2020 | Staff  | 2 | A | Possibly related, to each other and to Cluster 1 |
| 7 | 6/29/2020 | Staff  | 2 | A |
| 8 | 7/15/2020 | Staff  | 3 | B | Highly related |
| 9 | 7/17/2020 | Staff  | 3 | B |
| 10 | 7/27/2020 | Staff | 4 | C | Highly related |
| 11 | 7/28/2020 | Staff | 4 | C |
| 12 | 7/28/2020 | Staff | 4 | C |
| 13 | 7/29/2020 | Staff | 4 | C |
| 14 | 8/3/2020 | Staff  | 4 | C |
| 15 | 7/29/2020 | Staff | 4 | C |
| 16 | 7/6/2020 | Staff  | 5 | C | Unrelated |
| 17 | 7/13/2020 | Staff  | 5 | C |
| 18 | 7/13/2020 | Staff  | 5 | C |
| 19 | 7/31/2020 | Staff  | 6 | C |
| 20 | 7/31/2020 | Staff  | 6 | C |
| 21 | 7/28/2020 | Staff | 7 | D | Highly related |
| 22 | 7/27/2020 | Staff | 7 | D |
| 23 | 6/30/2020 | Staff  | 8 | E | Low coverage |
| 24 | 6/30/2020 | Staff  | 8 | E |
| 25 | 7/3/2020 | Staff | 9 | F | Unrelated |
| 26 | 7/31/2020 | Staff | 9 | F |
| 27 | 6/30/2020 | Staff | 10 | G | Unrelated |
| 28 | 6/30/2020 | Staff | 10 | G |
| 29 | 7/7/2020 | Staff | 10 | G |
| 30 | 7/6/2020 | Staff | 11 | H | Highly related |
| 31 | 7/6/2020 | Staff | 11 | H |
| 32 | 9/9/2020 | Staff | 12 | I | Highly related |
| 33 | 9/11/2020 | Staff | 12 | I |
| 34 | 9/9/2020 | Staff | 13 | J | Unrelated |
| 35 | 9/10/2020 | Staff | 13 | J |
| 36 | 9/9/2020 | Staff | 14 | K | Highly related |
| 37 | 9/10/2020 | Staff | 14 | K |
| 38 | 11/12/2020 | Patient | 15 | L | Highly related |
| 39 | 11/14/2020 | Staff | 15 | L |
| 40 | 12/7/2020 | Staff | 16 | M | Unrelated |
| 41 | 12/7/2020 | Staff | 16 | M |
| 42 | 11/23/2020 | Patient | 17 | M | Low coverage |
| 43 | 12/9/2020 | Patient | 18 | N | Unrelated to other cluster samples |
| 44 | 12/2/2020 | Staff | 18 | N | Low coverage |
| 45 | 12/7/2020 | Staff | 18 | N | Highly related  |
| 46 | 12/2/2020 | Parent | 18 | N |
| 47 | 11/30/2020 | Staff | 18 | N | Highly related |
| 48 | 11/25/2020 | Staff | 19 | N |
| 49 | 12/9/2020 | Staff | 20 | O | Highly related to Sample 51; Possibly related to Sample 52 |
| 50 | 12/11/2020 | Staff | 20 | O | Low coverage |
| 51 | 12/11/2020 | Staff | 20 | O | Highly related to Sample 49; Possibly related to Sample 52 |
| 52 | 12/14/2020 | Staff | 20 | O | Possibly related to Samples 49 and 51 |
| 53 | 12/16/2020 | Staff | 20 | O | Unrelated to other cluster samples |
| 54 | 12/17/2020 | Staff | 20 | O | Unrelated to other cluster samples |
| 55 | 12/7/2020 | Staff | 21 | P | Unrelated to 57 and 58 |
| 56 | 12/8/2020 | Staff | 21 | P | Low coverage |
| 57 | 12/8/2020 | Staff | 21 | P | Unrelated to 55 and 58 |
| 58 | 12/14/2020 | Staff | 21 | P |  Unrelated to 55 and 57 |
| 59 | 12/16/2020 | Staff | 22 | Q | Highly related |
| 60 | 12/15/2020 | Staff | 22 | Q |
| 61 | 12/15/2020 | Staff | 22 | Q |
| 62 | 12/18/2020 | Staff | 22 | Q |
| 63 | 12/17/2020 | Staff | 23 | R | Unrelated |
| 64 | 12/17/2020 | Staff | 23 | R |
| 65 | 12/22/2021 | Staff | 24 | S | Unrelated |
| 66 | 12/23/2021 | Staff | 24 | S |
| 67 | 12/26/2021 | Staff | 24 | S |
| 68 | 1/3/2021 | Patient | 25 | T | Unrelated to 70 |
| 69 | 1/2/2021 | Staff | 25 | T | Low coverage |
| 70 | 1/4/2021 | Staff | 25 | T | Unrelated to 68 |

**Supplementary Figure 1.** Histograms of pairwise distances generated for different time periods and for the combined data set. The highly related samples correspond to symmetric difference bins 0 and 1 of the histograms, separated by the vertical dash line from the rest of the distributions.

