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References
1. GISAID/Institut Pasteur de Dakar. Phylodynamics of pandemic coronavirus in west Africa. 2021 [cited 2021 Apr 5]. https://www.gisaid.org/phylodynamics/west-africa
2. Wilkinson E, Giovannetti M, Tegally H, San JE, Lessells R, Cuadros D, et al. A year of genomic surveillance reveals how the SARS-CoV-2 pandemic unfolded in Africa. Science. 2021;374:423-31. https://doi.org/10.1126/science.abj4336
3. Wruck W, Adjaye J. Detailed phylogenetic analysis tracks transmission of distinct SARS-COV-2 variants from China and Europe to West Africa. Sci Rep. 2021;11:21108. https://doi.org/10.1038/s41598-021-00267-w
4. Harvey WT, Carabelli AM, Jackson B, Gupta RK, Thomson EC, Harrison EM, et al.; COVID-19 Genomics UK (COG-UK) Consortium. SARS-CoV-2 variants, spike mutations and immune escape. Nat Rev Microbiol. 2021;19:409–24. https://doi.org/10.1038/s41579-021-00573-0
5. Sander AL, Yadouleton A, De Oliveira Filho EF, Tchibozo C, Houkankrin G, Badou Y, et al. Mutations associated with SARS-CoV-2 variants of concern, Benin, early 2021. Emerg Infect Dis. 2021;27:2889–903. https://doi.org/10.3201/eid2711.211353
6. World Health Organization. COVID-19 situation update for the WHO African Region, 26 August 2020 [cited 2020 Dec 26]. https://apps.who.int/iris/bitstream/handle/10665/334003/SITREP_COVID-19_WHOAFRO_20200826-eng.pdf
7. Ariyo OE, Oladipo EK, Osasona OG, Obe O, Olomojobi F. COVID-19 vaccines and vaccination: how prepared is Africa? Pan Afr Med J. 2021;39:107. https://doi.org/10.11604/pamj.2021.39.107.27912
8. Tsanni A. Covid-19: Africa scrambles to increase genomic testing capacity as variants spread. BMJ. 2021;373:n1122. https://doi.org/10.1136/bmj.n1122

Probable Transmission of SARS-CoV-2 Omicron Variant in Quarantine Hotel, Hong Kong, China, November 2021

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We report detection of severe acute respiratory syndrome coronavirus 2 Omicron variant (B.1.1.529) in an asymptomatic, fully vaccinated traveler in a quarantine hotel in Hong Kong, China. The Omicron variant was also detected in a fully vaccinated traveler staying in a room across the corridor from the index patient, suggesting transmission despite strict quarantine precautions.

A new variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), B.1.1.529, was identified in Botswana and South Africa in early November 2021 and was designated as variant of concern (VOC) Omicron by the World Health Organization on November 26, 2021 (1). As of December 1, 2021, ∼220 sequences were available on GISAID (https://www.gisaid.org), and this variant has been detected in countries in Africa and beyond since mid-November (2,3). This variant contains >30 spike protein amino acid mutations that might be associated with increased transmissibility, severity, and capacity for immune escape. With supporting evidence of epidemiologic and molecular epidemiologic findings, we report the probable transmission of Omicron in a quarantine hotel in Hong Kong, China. We also compare its mutational profile with other VOCs and variants of interest.

Two cases of infection with VOC Omicron (cases A and B) were detected in Hong Kong. Case-patient A arrived in Hong Kong from South Africa on November 11, 2021, and case-patient B arrived in Hong Kong from Canada on November 10, 2021. Both case-patients had previously received 2 vaccine doses (Pfizer-BioNTech, https://www.pfizer.com); the second dose was given on June 4, 2021, for case-patient A and on May 25, 2021, for case-patient B. Both case-patients tested negative by reverse transcription PCR (RT-PCR) for SARS-CoV-2 within 72 hours before arrival. On arrival at the Hong Kong...
airport, both case-patients stayed in the same quarantine hotel and had rooms across the corridor from each other on the same floor.

Case-patient A showed a positive result for SARS-CoV-2 without symptoms on November 13, 2021 (cycle threshold \([C_t]\) value 18). He was hospitalized and isolated the next day. Case-patient B had mild symptoms develop on November 17, 2021. He showed a positive result for SARS-CoV-2 (\(C_t\) value 19) on November 18, 2021, and was hospitalized on the same day. The 2 \(C_t\) values indicate high viral loads. None of the 12 persons staying in nearby rooms on the same floor during the study or related hotel staff have tested positive in repeated tests for SARS-CoV-2 (4).

Viral genomes deduced from these 2 SARS-CoV-2–positive cases differed only by 1 nt. Retrospective investigation, including closed-circuit television camera footage, confirmed that neither case-patient left their room during the quarantine period. No items were shared between rooms, and other persons did not enter either room. The only time the 2 quarantined persons opened their respective doors was to collect of food that was placed immediately outside each room door. The only other time they might have opened their doors would be for RT-PCRs, which were conducted in 3-day intervals. However, because these 2 case-patients arrived 1 day apart, it is unlikely that they would be tested on the same day. Airborne transmission across the corridor is the most probable mode of transmission.

**Figure.** Detection of severe acute respiratory syndrome coronavirus 2 Omicron variant in 2 patients (cases A and B) in Hong Kong, China, November 2021. A) Phylogenetic time tree of Omicron nucleotide sequences using an early severe acute respiratory syndrome coronavirus sequence as a reference sequence (Wuhan-Hu-1/2019; GenBank accession no. MN908947.3). B) Comparison of Omicron variant mutations in case A to other variants; red indicates VOC and gray VOI (Appendix, https://wwwnc.cdc.gov/EID/article/28/2/21-2422-App1.pdf). Text colors indicate mutations found in NTD (blue), RBD (orange), FP (purple), and HR1 (green). Lane 1, case A; 2, Alpha (B.1.1.7); 3, Beta (B.1.351); 4, Delta (B.1.617.2); 5, Gamma (P1); 6, Epsilon (B.1.427/429); 7, Eta (B.1.525); 8, Iota (B.1.526); 9, Kappa (B.1.617.1); 10, Lambda (C.37); 11, Mu (B.1.617.2); 12, Theta (P.3); 13, Zeta (P.2), E, envelope; FP, fusion peptide; HR1, heptad repeat 1; M, matrix; NSP, nonstructural protein; NTD, N-terminal domain; RBD, receptor-binding domain; S, spike; VOC, variant of concern; VOI, variant of interest.
We sequenced complete SARS-CoV-2 genomes from case-patients A and B (Appendix, https://wwwnc.cdc.gov/EID/article/28/2/21-2422-App1.pdf) and confirmed that these genomes were VOC Omicron (Pango lineage B.1.1.529) (Figure, panel A). Viral sequences from these 2 case-patients differed by only 1 nt. Viral sequence from case-patient A was highly similar to those of the first few reported Omicron cases identified in South Africa and Botswana (Appendix Table 1). Because many countries have just reported detection of this VOC (https://www.gisaid.org/hcov19-variants), the actual genetic diversity of this virus lineage requires further investigations.

The long branch of Omicron clade in the phylogenetic tree is attributed to the large number of mutations (Figure, panel A). Nonsynonymous mutations were identified in the spike (S)–encoding (n = 35) and other viral protein–encoding (n = 22) regions (Figure, panel B). Among the nonsynonymous mutations in the S protein, 43% (n = 15) were also identified in other VOCs/variants of interest, and 31% (n = 11) were found only in VOCs (Alpha, n = 6; Beta, n = 4; Gamma, n = 5; Delta, n = 4). Some of the point mutations and deletions found in other regions are not novel and can also be found in other variants at different frequencies (Appendix Table 2). Among these non-S mutations, NSP4-T492I, NSP6-S106del, NSP6-G107del, NSP12-P323L, N-P13L, N-R203K, and N-G204R are commonly found in SARS-CoV-2 variants.

The laboratory and epidemiologic features of the Omicron variant are yet to be fully characterized and cannot be determined on the basis of sequence features alone. Nonetheless, compared with other VOCs, the number of mutations found in the spike of the Omicron variant is unprecedented. This finding results in false-negative results in some diagnostic RT-PCRs specific for the S gene (3). Many of the mutations found in the S protein are known to alter SARS-CoV-2 antigenicity and transmissibility (5). The R203K and G204R mutations in the nucleocapsid protein are also associated with enhanced virus replication (6).

It is not known whether these detected mutations might have affected the effectiveness of existing vaccines and virus transmissibility. However, detection of Omicron variant transmission between 2 fully vaccinated persons across the corridor of a quarantine hotel has highlighted this potential concern. Further experimental characterizations and epidemiologic investigations of this newly found VOC are urgently needed. Increased precautions or additional measures might be warranted while awaiting more data.

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References
1. World Health Organization. Tracking SARS-CoV-2 variants, 2021 [cited 2021 Nov 27]. https://www.who.int/en/activities/tracking-SARS-CoV-2-variants
2. Callaway E. Heavily mutated coronavirus variant puts scientists on alert. Nature. 2021;600:21 [cited 2021 Dec 2]. https://www.nature.com/articles/d41586-021-03552-w
3. World Health Organization. Classification of Omicron (B.1.1.529): SARS-CoV-2 variant of concern, 2021 [cited 2021 Nov27]. https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern
4. Hong-Kong-Government. CHP provides update on latest investigations on COVID-19 imported cases 12388 and 12404, 2021 [cited 2021 Nov 26]. https://www.info.gov.hk/gia/general/202111/22/P2021112200897.htm
5. Tao K, Tzou PL, Noushin J, Gupta RK, de Oliveira T, Kosakovsky Pond SL, et al. The biological and clinical significance of emerging SARS-CoV-2 variants. Nat Rev Genet. 2021:22:757–73. https://doi.org/10.1038/s41576-021-00408-x
6. Wu H, Xing N, Meng K, Fu B, Xue W, Dong P, et al. Nucleocapsid mutations R203K/G204R increase the infectivity, fitness, and virulence of SARS-CoV-2. Cell Host Microbe. 2021;31931-3128(21)00511-4.

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Additional Methods

Sequencing

Respiratory swab samples from cases A and B were subjected to next-generation sequencing. RNA samples were sent to a World Health Organization reference laboratory at the University of Hong Kong for full-genome analyses (Institutional Review Board no. UW 20–168). We deduced near full-length genomes from the samples by using a described Illumina sequencing protocol (1,2). Briefly, virus genome was reverse transcribed with multiple gene-specific primers targeting different regions of the viral genome. The synthesized cDNA was then subjected to multiple overlapping 2-kb PCRs for full-genome amplification. PCR amplicons obtained from the same specimen were pooled and sequenced by using the iSeq sequencing platform (Illumina). Sequencing library was prepared by using Nextera XT (illumine). Generated sequencing reads were mapped to a reference virus genome by using the Burrow–Wheeler Aligner (3), and genome consensus was generated by using iVar with the PCR primer trimming protocol (minimum sequence depth >10 and minimum Q value of 30) (4). The deduced sequences are available at GISAID (Accession nos. EPI_ISL_6716902 and EPI_ISL_6716890).

Phylogenetic Analysis

The 2 sequences from Hong Kong were analyzed together with a set of representative sequences from other lineages, including all sublineages under B.1.1 (Pango lineage) and all variants of concern/variants of interest lineages. The sequences were retrieved from the presubsampled prealigned open database from Nextstrain (https://docs.nextstrain.org/projects/ncov/en/latest/reference/remote_inputs.html). The maximum-likelihood phylogenies were estimated by using IQ-TREE version 2.1.3 (5) and the general time reversible + empirical base frequencies + FreeRate model of with number of
categories of 2 nucleotide substitution model with Wuhan-Hu-1 (GenBank accession no. MN908947.3) as the outgroup. Dating of the tree were performed by using IQ-TREE LSD2 with specifications “–date-root 2019-12-26–date-ci 100–date-options "-l -1”.”

**Mutation Analysis**

The lineages defining mutations (or lineage specific mutations) for different variants of concern/variants of interest (Figure, panel B) were curated from 3 public databases (https://covariants.org/shared-mutations, https://github.com/cov-lineages/constellations, and https://outbreak.info/). Detailed analyzing scripts used in the study can be accessed in a GitHub repository (https://github.com/Leo-Poon-Lab/Detection-of-B.1.1.529-variant-in-Hong-Kong).

**References**

1. Choi EM, Chu DK, Cheng PK, Tsang DN, Peiris M, Bausch DG, et al. In-flight transmission of SARS-CoV-2. Emerg Infect Dis. 2020;26:2713–6. PubMed https://doi.org/10.3201/eid2611.203254

2. Sit TH, Brackman CJ, Ip SM, Tam KW, Law PY, To EM, et al. Infection of dogs with SARS-CoV-2. Nature. 2020;586:776–8. PubMed https://doi.org/10.1038/s41586-020-2334-5

3. Vasimuddin M, Misra S, Li H, Aluru S. Efficient architecture-aware acceleration of BWA-MEM for multicore systems. In: 33rd IEEE International Parallel and Distributed Processing Symposium (IPDPS), 2019. Rio de Janeiro, May 20–24, 2019. p. 314–24.

4. Grubaugh ND, Gangavarapu K, Quick J, Matteson NL, De Jesus JG, Main BJ, et al. An amplicon-based sequencing framework for accurately measuring intrahost virus diversity using PrimalSeq and iVar. Genome Biol. 2019;20:8. PubMed https://doi.org/10.1186/s13059-018-1618-7

5. Minh BQ, Schmidt HA, Chernomor O, Schrempf D, Woodhams MD, von Haeseler A, et al. IQ-TREE 2: new models and efficient methods for phylogenetic inference in the genomic era. Mol Biol Evol. 2020;37:1530–4. PubMed https://doi.org/10.1093/molbev/msaa015
**Appendix Table 1.** Nucleotide divergences between viral sequences of case A with other Omicron virus sequences

| Reference sequence (case A) | No. nucleotide divergences* | No. nucleotide divergences in spike gene* |
|----------------------------|-----------------------------|----------------------------------------|
| hCoV-19/Botswana/R40B59_BHP_3321001248/2021| 1                          | 0                                     |
| hCoV-19/Botswana/R40B60_BHP_3321001247/2021| 1                          | 0                                     |
| hCoV-19/South_Africa/NICD-N21607-DX64624/2021| 1                          | 1                                     |
| hCoV-19/South_Africa/NICD-N21600-DX03569/2021| 2                          | 2                                     |
| hCoV-19/South_Africa/NICD-N21602-DX040380/2021| 2                          | 2                                     |
| hCoV-19/South_Africa/NICD-N21605-DX64490/2021| 3                          | 2                                     |
| hCoV-19/South_Africa/NICD-N21603-DX64204/2021| 4                          | 2                                     |
| hCoV-19/South_Africa/NICD-N21604-DX64219/2021| 6                          | 2                                     |
| USA/ID-CDC-LC0011682/2021 (B.1.1.519)       | 55                         | 27                                    |
| Wuhan-Hu-1/2019                         | 54                         | 30                                    |

*Ambiguous or deleted nucleotide regions in these published sequences are excluded in the analysis.
†Viral sequence of case B differs from that of case A by 1 nt (nt position G6167C) and this mutation cannot be found in other reported Omicron virus variant sequences.

**Appendix Table 2.** Nonsynonymous mutations found in VOC Omicron

| Gene | Mutation | Frequency in GISAID, % |
|------|----------|-----------------------|
| NSP3 | K38R     | 0.01                  |
| NSP3 | V1069I   | 0.02                  |
| NSP3 | S1265del | 0.02                  |
| NSP3 | L1266I   | 0.02                  |
| NSP3 | A1892T   | 0.00                  |
| NSP4 | T492I    | 46.49                 |
| NSP5 | P132H    | 0.01                  |
| NSP6 | L105del  | 0.02                  |
| NSP6 | S106del  | 25.59                 |
| NSP6 | G107del  | 25.59                 |
| NSP6 | I189V    | 0.03                  |
| NSP12| P323L    | 96.94                 |
| NSP14| I42V     | 0.00                  |
| Spike| A67V     | 0.37                  |
| Spike| H69del   | 21.90                 |
| Spike| V70del   | 21.93                 |
| Spike| T95I     | 20.79                 |
| Spike| G142D    | 32.16                 |
| Spike| V143del  | 0.13                  |
| Spike| Y144del  | 21.66                 |
| Spike| Y145del  | 19.25                 |
| Spike| N211del/L212I | 0.02/0.01 |
| Spike| G339D    | 0.01                  |
| Spike| S371L    | 0.00                  |
| Spike| S373P    | 0.01                  |
| Spike| S375F    | 0.00                  |
| Spike| K417N    | 0.86                  |
| Spike| N440K    | 0.17                  |
| Spike| G446S    | 0.01                  |
| Spike| S477N    | 1.36                  |
| Spike| T478K    | 51.35                 |
| Spike| E484A    | 0.02                  |
| Spike| Q493R    | 0.01                  |
| Spike| G496S    | 0.01                  |
| Spike| Q498R    | 0.00                  |
| Spike| N501Y    | 24.94                 |
| Spike| Y505H    | 0.00                  |
| Spike| T547K    | 0.01                  |
| Spike| D614G    | 98.81                 |
| Spike| H655Y    | 2.32                  |
| Spike| N679K    | 0.10                  |
| Spike| P681H    | 23.51                 |
| Spike| N764K    | 0.01                  |
| Spike| D796Y    | 0.08                  |
| Spike| N856K    | 0.00                  |
| Spike| Q954H    | 0.00                  |
| Gene            | Mutation | Frequency in GISAID, % |
|-----------------|----------|-----------------------|
| Spike           | N969K    | 0.00                  |
| Spike           | L981F    | 0.00                  |
| Matrix          | D3G      | 0.08                  |
| Matrix          | Q19E     | 0.00                  |
| Matrix          | A63T     | 0.01                  |
| Nucleocapsid    | P13L     | 0.65                  |
| Nucleocapsid    | E31del   | 0.00                  |
| Nucleocapsid    | R32del   | 0.00                  |
| Nucleocapsid    | S33del   | 0.00                  |
| Nucleocapsid    | R203K    | 28.70                 |
| Nucleocapsid    | G204R    | 27.10                 |
| Envelope        | T9I      | 0.09                  |

*NNSP, nonstructural protein.

**Appendix Table 3. GISAID sequences used in this study**

| Accession no.    | Originating laboratory            | Submitting laboratory         | Authors                                                                 |
|------------------|----------------------------------|-------------------------------|-------------------------------------------------------------------------|
| EPI_ISL_6640916, | Botswana Harvard HIV Reference   | Botswana Harvard HIV Reference| Sikhulile Moyo, Wonderful T. Choga, Dorcas                             |
| EPI_ISL_6640917, |                                   |                               | Maruapula, Keoratlie Ntshambiwa, Sefetogi Ramaologa, Thongbotho Mphoyakgos, Botumelo Zuze, Botshelo Radibe, Legodile Kooepile, Ontiametse T. Bareng, Pamela Smith-Lawrence, Kgomotso Moruisi, Roger Shapiro, Shahin Lockman, Joseph Makhema, Mphaphi B. Mbulawa, Mosepele, Simani Gasetsiwe |
| EPI_ISL_6640919  | Botswana Reference Laboratory    |                               |                                                                          |
| EPI_ISL_6647956  | Lancet laboratory                | National Institute for        | D.G. Amoako, J. Everatt,                                              |
| EPI_ISL_6647957  |                                   | Communicable Diseases of the  | C. Scheepers, A. Glass,                                                |
| EPI_ISL_6647958  |                                   | National Health Laboratory    | Viana R, Mohale T.N. Ntuli,                                           |
| EPI_ISL_6647959  |                                   |                               | B. Mahangu, A. Mnguni,                                                |
| EPI_ISL_6647960  |                                   |                               |                                                                          |
| EPI_ISL_6647962  |                                   |                               |                                                                          |