Three SARS-CoV-2 recombinants identified in Brazilian children

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Short Report

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Abstract

Since the emergence of the variant of concern (VOC) B.1.1.529 (Omicron) in November 2021[1], nearly 100 sublineages have been assigned by Pango. Recently, the co-circulation of Omicron and Delta lineages, as well as its diverse set of sublineages, has brought to attention the identification of several recombinant events. A putative new recombinant and two XE recombinants were identified in children by the GENOV surveillance program (https://dasa.com.br/en/genov/) from Dasa, Brazil. All three children haven't traveled abroad nor their relatives, indicating that the infections by recombinants likely occurred in São Paulo city.

Full Text

Since the emergence of the variant of concern (VOC) B.1.1.529 (Omicron) in November 2021[1], nearly 100 sublineages have been assigned by Pango[2,3]. Recently, the co-circulation of Omicron and Delta lineages, as well as its diverse set of sublineages, has brought to attention the identification of several recombinant events. A dynamical nomenclature system for the designation of new lineages was created by the Pango network committee, in which recombinants start with an X letter[4]. Currently, there are 3 Delta/Omicron (XD, XF, XS) and 13 Omicron BA.1*/BA.2 (XE, XG, XH, XJ, XK, XL, XM, XN, XP, XQ, XR, XT, and XU) recombinants, according to the Pango designation, release v1.8 (https://github.com/cov-lineages/pango-designation).

A putative new recombinant and two XE recombinants were identified in children by the GENOV surveillance program (https://dasa.com.br/en/genov/) from Dasa, Brazil. Next-generation sequencing (NGS) using the Illumina COVIDSeq Test on the NovaSeq 6000 (Illumina, CA, USA), and analyzed with Illumina® DRAGEN Covid Lineage App (version 3.5.9) from BaseSpace™ Sequence Hub.

Three years old male child from São Paulo city, Brazil, presented an unassigned lineage according to standard pipeline classification. The sample was collected on Feb 16, 2022, and the complete genome sequencing resulted in a median coverage of 1,379 (99.39% over 30x) and 99.59% of non-N bases, with no detected sign of co-infection or contamination of negative controls. The consensus sequence was deposited on GISAID[5] under the ID EPI_ISL_12055062 (hCoV-19/Brazil/SP-DASA828822284657/2022).

Further analysis with Nextclade Web (version 1.14.0) resulted in a recombinant lineage with XM Pango classification, however, a few reversions and private mutations could be identified (**Figure 1a**). The presence of the labeled mutation C17410T from the 21L clade (that includes BA.2) suggested a breakpoint different from the XM lineage (https://github.com/cov-lineages/pango-designation/issues/472). The sc2rf tool (https://github.com/lenaschimmel/sc2rf) was used to screen potential breakpoints and compare the putative new recombinant with XE, XM, and XJ lineages (**Figure 1b**). A single breakpoint was detected between positions 15714 and 17410 in the ORF1B of the new recombinant.

A search for similar sequences in the public databases and their relationship with known recombinants in the phylogenetic tree was done with the UShER[6] utility from the UCSC Genome Browser group (https://genome.ucsc.edu/cgi-bin/hgPhyloPlace). The new recombinant did not cluster with XM samples but was allocated separately in a non-resolved and multifurcated branch containing a miscellaneous of non-designated BA.1*/BA.2 recombinants (**Figure 2**). Samples from Malaysia, India, Denmark, England, and Japan presented the same estimated single breakpoint of the new recombinant, between positions 15714 and 17410 at the ORF1B.

However, these samples found by UsHER diverge mostly by substitutions related to the BA.1 and may represent different potential recombinant lineages. The Brazilian sample instead, presents substitutions such as ORF1a:T4174I and ORF1a:A3615V that could characterize a BA.1.14.1 lineage (https://github.com/cov-lineages/pango-designation/issues/506). The BA.1.14.1 lineage has been mostly found in the Brazilian population, with an estimated 4% relative growth advantage reported by CoV-Spectrum[7] (accession date 2022-04-27). Sample resequencing resulted in an identical consensus sequence with a median coverage of 2032 (99.56% over 30x) and 99.59% of non-N bases.

According to the PANGO designation, the minimum number of high-quality sequences to designate a new lineage is five, and at least 50 sequences are expected for significant recombinant lineages[8]. The identified SARS-CoV-2 BA.1.14.1/BA.2 recombinant will be continuously monitored by the GENOV surveillance team.

Additionally, two XE recombinants were identified by the GENOV surveillance project in April 2022 and were deposited in GISAID under IDs EPI_ISL_12103644 and EPI_ISL_12103643. These samples were from twins, female and male children of 10 years old from São Paulo city, both collected on March 11, 2022. The EPI_ISL_12103644 presented a median coverage of 1,623 (99.5% over 30x) with 99.59% of non-N bases, and EPI_ISL_12103643 a median coverage of 1,190 (98.76% over 30x) with 99.48% of non-N bases. Both presented an unlabeled private mutation at ORF1a:I2010V identified by Nextclade. At present, these are the first cases of XE in children deposited at GISAID, and the other two cases of XE in adults from São Paulo state (EPI_ISL_11294819 - March 22, 2022, and EPI_ISL_12466897 - April 18, 2022) also have been reported at GISAID (accession date: May 05, 2022).

All three children haven't traveled abroad nor their relatives, indicating that the infections by recombinants likely occurred in São Paulo city.

Declarations

Ethics approval:

The COVID-19 Genomic surveillance project that identified these 3 recombinants described in the manuscript was approved by the Ethical Committe from Hospital Nove de Julho, CAAE 45540421.0.0000.5455.

Competing interests:

The authors declare no competing interests.

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Figures

Figure 1

Characteristics of the consensus sequence from the putative new Brazilian recombinant. **(a)** Substitutions and private mutations described by Nexclade Web (version 1.14.0) regarding XM classification of hCoV-19/Brazil/SP-DASA828822284657/2022. **(b)** Output from the sc2rf tool that highlights a different single breakpoint compared to XE, XM, and XJ samples.

Figure 2

UShER placement for the recombinant EPI_ISL_12055062, colored in red, with https://genome.ucsc.edu/cgi-bin/hgPhyloPlace (accession date 2022-04-28).