

Unnatural evolutionary processes of SARS-CoV-2 variants and possibility of deliberate natural selection

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16 **Abstract**

17 Over the past three years, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has repeatedly
18 caused pandemics, generating various mutated variants ranging from Alpha to Omicron. In this study, we
19 aimed to clarify the evolutionary processes leading to the formation of SARS-CoV-2 Omicron variants,
20 focusing on Omicron variants with many amino acid mutations in the spike protein among SARS-CoV-2
21 isolates. To determine the order of mutations leading to the formation of the SARS-CoV-2 Omicron variants,
22 we compared the sequences of 129 Omicron BA.1-related, 141 BA.1.1-related, and 122 BA.2-related isolates,
23 and attempted to clarify the evolutionary processes of SARS-CoV-2 Omicron variants, including the order of
24 mutations leading to their formation and the occurrence of homologous recombination. As a result, we
25 concluded that the formation of a part of Omicron isolates BA.1, BA.1.1, and BA.2 was not the product of
26 genome evolution, as is commonly observed in nature, such as the accumulation of mutations and homologous
27 recombinations. Furthermore, the study of 35 recombinant isolates of Omicron variants BA.1 and BA.2
28 confirmed that Omicron variants were already present in 2020. The analysis showed that Omicron variants
29 were formed by an entirely new mechanism that cannot be explained by previous biology, and knowing how
30 the SARS-CoV-2 variants were formed prompts a reconsideration of the SARS-CoV-2 pandemic.

31 **1 Introduction**

32
33 COVID-19, the coronavirus disease 2019, caused by severe acute respiratory syndrome coronavirus 2 (SARS-
34 CoV-2), was first reported in December 2019 in Wuhan, China (1). This emerging infectious disease was
35 unprecedentedly fast, spreading worldwide, leading the World Health Organization (WHO) to declare a global
36 pandemic of COVID-19 on March 11, 2020 (<https://www.who.int/>). SARS-CoV-2, belonging to
37 betacoronavirus subgroup B, has a single-stranded positive-sense RNA genome that codes for ten genes,
38 ultimately producing 26 proteins according to an annotation of NCBI Reference Sequence: NC_045512.2. Its
39 genome size varies from 29.8 to 29.9 kb. It consists of four structural proteins: spike (S), envelope (E),
40 membrane (M), and nucleocapsid (N) proteins (2, 3). In the structural proteins, the S protein as the surface
41 glycoprotein is the largest protein, being approximately 180 kDa, and consisting of two subunits, S1 and S2. It
42 mediates membrane fusion and ultimately facilitates virus entry. The receptor-binding domain (RBD) (amino

43 acid residues 319-541) of the S1 subunit interacts with angiotensin - converting enzyme 2 (ACE2), binding to
44 its peptidase domain (4, 5).

45

46 Over the three years from 2019 to 2022, SARS-CoV-2 was re-accelerated by new variants that emerged over
47 several months in various geographical regions and disseminated throughout the world, to induce the pandemic
48 repeatedly.

49

50 In the early stage of the first pandemic, the most impactful mutation of SARS-CoV-2 was the non-synonymous
51 mutation D614G in the S protein. This mutation, which was not present in the ancestral lineage that caused the
52 Wuhan outbreak, quickly became dominant worldwide (6). Soon after, the variant of concern, B.1.1.7 : 20I
53 (Alpha, V1), the lineage B.1.1.7 (clade 501.YV1), or Alpha, characterized by 17 unique mutations containing
54 ten amino acid differences in the S protein, was first detected in southeastern England in late September 2020
55 (7) and expanded rapidly across the United Kingdom to become predominant during early 2021, spreading to
56 most European countries with similar success. By November 2021, local transmission of this lineage had been
57 reported in 175 countries (8). Shortly after, the emergence of variant strains of SARS-CoV-2 Alpha, variants
58 B.1.351 : 20H (Beta, V2), was identified in October 2020, which was first detected in the Eastern Cape province
59 of South Africa from specimens collected in early August. This Beta variant spread within South Africa and was
60 considered to have displaced the other SARS-CoV-2 lineages circulating there (9). Then, the variant P.1: 20J
61 (Gamma, V3) was identified in Brazil in December 2020, thought to have evolved in Brazil. Health officials in
62 Japan first reported it publicly on January 10, 2021, after identifying the Gamma variant in four Brazilian
63 travelers at Haneda Airport in Tokyo, Japan (10).

64 At about the same time, the Delta variant (Pango lineage designation B.1.617.2), which was first detected in
65 India in February 2021, and the Mu variant, also known as lineage B.1.621 first detected in Colombia in January
66 2021, were reported (11, 12). While the lambda variant (Pango lineage designation C.37), was detected in Peru
67 in August 2020, but designated in June 15, 2021 by WHO (13, 14).

68

69 Almost one year later, regarding these emergences of variants of concern, Omicron (phylogenetic assignment
70 of named global outbreak (Pango) lineage designation B.1.1.529; BA.1, Nextstrain clade 21K) was a variant of
71 SARS-CoV-2 first reported to WHO by the Network for Genomics Surveillance in South Africa on November
72 24, 2021 (15, 16) with more than 50 amino acids changes when compared with the first reported strain Wuhan-
73 Hu-H1 (NCBI Reference Sequence: NC_045512.2.), and 39 of these amino acids difference were observed in
74 the S protein. This variant was first detected in Botswana and became the predominant circulating variant
75 worldwide (17).

76 In the United States, the San Francisco Department of Public Health confirmed that a case of COVID-19 among
77 individuals in California was caused by Omicron variant BA.1, carried by a traveler who returned from South
78 Africa on November 22, 2021 (<https://www.cdc.gov/media/releases/2021/s1201-Omicron-variant.html>). Then,
79 the first Omicron sub-lineage BA.1 expanded rapidly and replaced the Delta variant (18).

80 Less than two weeks later, the Omicron variant BA.1, the new Omicron variant, BA.2 lineage, showing 31
81 amino acids changes in the S protein when compared with the Wuhan-Hu-H1, was initially identified in
82 Denmark on December 5, 2021 (19). On February 22, 2022, WHO mentioned the Omicron sublineage BA.2
83 (<https://www.who.int/news/item/22-02-2022-statement-on-Omicron-sublineage-ba.2>), whereby the Omicron
84 variant of concern was currently the dominant variant circulating globally, replacing the Delta variant (Pango
85 lineage designation B.1.617.2) (https://www.who.int/docs/default-source/coronaviruse/2022-01-07-global-technical-brief-and-priority-action-on-Omicron---corr2.pdf?sfvrsn=918b09d_20), accounting for nearly all
86 sequences reported to GISAID. Then, as of March 16, 2023, WHO stated that the Omicron variants accounted
87 for over 98% of the publicly available viral sequences after February 2022 (<https://www.who.int/news/item/16-03-2023-statement-on-the-update-of-who-s-working-definitions-and-tracking-system-for-SARS-CoV-2-variants-of-concern-and-variants-of-interest>).

91 Omicron variants BA.1 and BA.2 were suggested to have expanded and diverged around October to December
92 2021, respectively. These mutants were estimated to have diverged from a common ancestor around February
93 to March 2021 (20). Since Omicron variants BA.1 and BA.2 share a common 14-amino acid mutation in the S

94 protein, the common ancestor of Omicron variants BA.1 and BA.2 may have already acquired the 14-amino
95 acid mutation in the S protein region around February to March 2021; however, no common ancestral strain has
96 been found in the international databases, and the strains may have acquired their mutations through different
97 pathways.

98 In this study, we attempted to clarify the evolutionary processes of the Omicron variant, which has two-times
99 more amino acid mutations in the S protein than other variants, by examining the rank order of introduced amino
100 acid mutations in the S protein.

101 2 Results

102 Each variant is considered to have arisen through an independent evolutionary pathway from isolates with the
103 D614G mutation in the S protein. Concerning the genetic variation in the S protein of these variants, most of the
104 mutations were non-synonymous (Fig. 1). There were no synonymous mutations in the Alpha, Beta, Gamma,
105 Delta, or Mu variants, but only one each in the Lambda and Omicron variants. Among these variants, the
106 Omicron variant (BA.1 lineage), which shows the greatest accumulation of mutations in the S protein, is
107 primarily non-synonymous in the S protein and has only one synonymous mutation, at c25000u. The
108 synonymous/non-synonymous ratio is abnormal, considering how human coronaviruses have mutated (See
109 Supplemental Figure 1).

110 At first, we considered the existence of the isolate of SARS-CoV-2, whose amino acid sequence in the S protein
111 contains the Omicron-BA.1-type mutation subsets, but one mutation position was not mutated and comprised
112 the original Wuhan-type amino acid sequence. We designated these isolates as BA.1-01. Each amino acid
113 sequence of the S protein region was named BA.1-0.1_S: amino acids of the Omicron-BA.1 type (Oaa) and
114 Wuhan type (Waa) and its position number (XXX) (Ex., BA.1-0.1_S:OaaXXXWaa), as described in Methods.
115 Then, the putative isolates bearing BA.1-0.1_S:OaaXXXWaa were searched for using the BLAST program
116 based on their amino acid sequences. In this search, we obtained the isolates whose identities showed 100%
117 matches with the query amino acid sequence except for SARS-CoV-2_human_USA_NY-
118 PV55373_2022(GenBank: ON246090.1), whose identity was 99.92%.

119 Surprisingly, we found that Omicron BA.1-0.1 isolates were detected at all mutation sites except N501Y (Fig.
120 2A). In the BA.1 lineage of the Omicron variant, there are Omicron isolates (BA.1.1) with the R346K mutation
121 seen in the Mu(m) variant (termed B.1.621), *i.e.*, BA.1_S can be defined as BA.1.1_S:K346R. We also
122 performed a BLAST search for isolates with amino acid sequences of BA.1-0.1.1_S:OaaXXXWaa, as described
123 in Methods. As a result, Omicron BA.1.1-subset-0.1 isolates were detected at all mutation sites except S373P
124 (Fig. 2B). Similar to the BA.1 lineage of the Omicron variant, in the BA.2 lineage of the Omicron variant,
125 isolates of BA.2-0.1 were found at all mutant sites except T478K and P681H in the S protein (Supplemental
126 Figure 2). The presence of these isolates refutes the establishment of Omicron strains through a continuous
127 evolutionary process by accumulating mutations. So, we could not determine which mutation occurred first or
128 last to form the Omicron variants. As shown in Fig. 2B, over half of the BA.1.1-0.1 isolates have the synonymous
129 mutation c21595u detected in the S protein. However, this does not help explain the order in which the c21595u
130 mutation arose. Curiously, in BA.1 strain isolates, this c21595u mutation was only detected in SARS-CoV-
131 2_human_USA_ID-CDC-LC0481844_2022 (GenBank: OM409228.1) and SARS-CoV-2_human_USA_MI-
132 CDC-ASC210597972_2022 (GenBank: OM396816.1). These isolates commonly lack the G339D mutation.
133 This synonymous mutation is in a mutation-prone hotspot location. Still, if the same mutation occurred
134 independently in different isolates, it is highly unnatural for the proportion of c21595u occurrences to be
135 significantly biased in the Omicron variants BA.1.1-0.1.

136 It has been reported that two different variants were infected in a single cell while establishing various SARS-
137 CoV-2 variants, causing homologous recombination in the process of viral RNA synthesis, resulting in multiple
138 variants. On considering that homologous recombination caused the isolates shown in Fig. 2, some of the
139 breakpoints at which strand changes occur by homologous recombination are too short (1nt, 2nt, 3nt, etc.) (Fig.
140 3 and Supplemental Figure 3). Therefore, it is unreasonable to employ homologous recombination as the basis
141 for establishing these isolates. Also, most of these isolates were found in the USA between 2021 and 2022;

142 however, considering that the most prevalent variant in the USA in August 2021 was the Delta variant, it is most
143 unlikely that it did not cause mutations such as T478K and D614G, which were already prevalent. It is
144 inconceivable that the oldest variants (such as T478K and D614G), which were no longer prevalent, were
145 sufficiently present to cause superinfection and be involved in homologous recombination. Also, most of these
146 isolates were isolated in the USA between 2021 and 2022. Still, given that the isolates primarily prevalent in the
147 USA in August 2021 were Delta variants, it is unlikely that an older type of variant without the T478K or D614G
148 mutation was present to cause superinfection and be involved in homologous recombination. This consideration
149 is supported by the fact that all of these BA.1-0.1 and BA.1.1-0.1 isolates retained the sequence of the BA.1
150 lineage in all regions except the S protein (Fig. 4). In addition, the fact that all of these BA.1-0.1 and BA.1.1-
151 0.1 strains retained the sequence of Omicron strain BA.1 except for the S protein also makes it unreasonable to
152 consider that these isolates arose by homologous recombination with an older type of mutant without the T478K
153 or D614G mutations (Fig. 4).

154 Furthermore, some of the BA.1 and BA.1-0.1 isolates have mutation subsets (synonymous: u10135c, ORF3:
155 L106F, N: D343G) up- and downstream of the S gene, and the u10135c and L106F (ORF3) mutations
156 correspond perfectly. Therefore, it is considered that homologous recombination between the BA.1 variant and
157 variants without these mutations did not occur during the mutants' formation processes (Fig. 4). The synonymous
158 mutation c2470u occurred in BA.1.1 compared with BA.1, and this c2470u mutation was retained by most,
159 excluding a few of the BA.1.1-0.1 isolates (SARS-CoV-2_human_USA_IL-CDC-ASC210695497_2022 :
160 GenBank: OM770362.1; SARS-CoV-2_human_USA_NY-CDC-LC0450936_2021: GenBank: OM228453.1) .
161 The synonymous mutation c2470u has also only been observed in a minimal number of BA.1-0.1 isolates
162 (SARS-CoV-2_human_USA_OR-CDC-LC0470830_2022: GenBank: OM367679.1; SARS-CoV-
163 2_human_USA_ID-CDC-LC0481844_2022: GenBank: OM409228.1; SARS-CoV-2_human_USA_MI-CDC-
164 ASC210597972_2022: GenBank:OM396816.1; SARS-CoV-2_human_USA_WI-CDC-LC0494047_2022:
165 GenBank: OM500517.1) . These results suggest that the establishment of BA.1-0.1 and BA.1.1-0.1 isolates
166 occurred independently. On the other hand, if reversion mutations caused each of these isolates with one amino
167 acid different to the Wuhan-type, these isolates could be detected by examining an astronomical number of
168 isolates. However, these virus strains were detected in the number of sequenced whole genomes (a limited
169 number), rather than in astronomical numbers examined. The fact that most of these mutations occurred without
170 synonymous mutations (Fig. 2) suggests that none of them arose as a result of trial-and-error random mutations
171 in nature. Few synonymous mutations are detected in some BA.1-0.1, BA.1.1-0.1, and BA.2-0.1 isolates (Fig.
172 2 and Supplemental Figure 2), as seen in other viruses (Supplemental Figure 1). The c25000u is the only
173 synonymous mutation that did not occur until BA.1, BA.1.1, BA.2, BA.1-0.1 BA.1.1-0.1, and BA.2-0.1 isolates
174 were formed and was not observed in previous variants such as alpha, beta, gamma, delta, etc. Nevertheless, it
175 is curious to find the occurrence of mutants with synonymous mutations such as c22120u, c24034u, c23635u,
176 c24448u, c21811u, a23884g, c22987u, c23609a, c23413u, c23896u, c22879u, u24097a, c23893u, c24442u,
177 u24847c, c24382u, c22264u, c22879u, c22480u, u21976c, c22480u, g24577a, and u23101c in BA.1.1, BA.1-
178 0.1, and BA.1.1-0.1 isolates (Fig. 2 Synonymous Others), and a22948g, c23635u, c21859u, c22945u, c23701u,
179 c22987u, a24433g, c23347u, u24640c, a24619g, c24865u, a23989g, u23047c, u24346c, c21811u, c21952u,
180 a22753u, c23635u, c24023u, c24382u, and c22572u in BA.2-0.1 isolates (Supplemental Figure 2 Synonymous
181 Others) after the formation of mutants with these subsets.

182 Although the only bias in our isolates collection, was only selection of isolates whose identities showed 100%
183 matches with the query amino acid sequence in the BLAST search, these curious tendencies were observed is
184 very interesting.

185 If two different viral variants infect a single cell simultaneously in the process of establishing various SARS-
186 CoV-2 variants, and if homologous recombination occurs during viral RNA synthesis between the Omicron
187 variant BA.1 lineage and BA.2 lineage, it is expected that there are variants caused by homologous
188 recombination between the BA.1 and BA.2 lineages.

189 Therefore, we also performed BLAST searches for isolates with mutant amino acid subsets of both the Omicron
190 variant BA.1 and BA.2 strains. We detected recombinant isolates of Omicron BA.1 and BA.2 lineages.

191 Surprisingly, the recombinant Omicron BA.1 and BA.2 lineages, SARS-CoV-2/human/PRI/PR-PR-UPRRP-
192 582/2020 (GenBank: ON928946.1), were already present in Puerto Rico in 2020. Omicron (B.1.1.529) is a
193 variant of SARS-CoV-2 first reported to WHO by the Network for Genomics Surveillance in South Africa on
194 November 24, 2021 (15, 16). It was first detected in Botswana and spread to become the predominant variant in
195 circulation worldwide (17). Following the appearance of the original B.1.1.529 variant, several subvariants of
196 Omicron emerged, including BA.1, BA.2, BA.3, BA.4, and BA.5 (21). After October 2022, two subvariants of
197 BA.5 called BQ.1 and BQ.1.1 emerged.

198 The question then arose about why a recombinant strain, SARS-CoV-2/human/PRI/PR-UPRRP-582/2020
199 (GenBank: ON928946.1), already existed in 2020. We searched for SARS-CoV-2 isolates prevalent in Puerto
200 Rico using the keywords "PRI", "PR-UPRRP", and "2020" in the NCBI search; nucleotide
201 (<https://www.ncbi.nlm.nih.gov/>). Consequently, we found 29 Omicron-associated sequences in the 127 hits
202 obtained (Fig. 5B). These results suggest that the SARS-CoV-2 variants bearing the amino acid sequences of
203 the S protein are identical to Omicron BA.1 and Omicron BA.2 variants, which were already prevalent in Puerto
204 Rico in 2020, with 15 isolates showing the complete Omicron BA.1+ R346K_mut-subset (BA1.1) , and 14
205 isolates showing a synonymous substitution of c21595u. Four isolates had an amino acid sequence of the S
206 protein that perfectly matched that of Omicron BA2 (BA.2_S), four isolates were Omicron BA.2-0.1 (BA.2-
207 S:K440N) and four isolates were Omicron BA.2-0.1 (BA.2-S:K440N)+F79S, BA.2-0.1 (BA.2-
208 S:K440N)+Q613H, BA.2-0.1 (BA.2-S:K440N)+212S+D215E and BA.2-0.1 (BA.2-S:K440N)+212S (Fig. 5B).

209

210 3 Discussion

211 Several hypotheses have been proposed in which the original SARS-CoV-2 virus resulted from an accidental
212 laboratory spill. With recent developments in biotechnology, many viruses, including coronaviruses, have been
213 artificially synthesized and used in various experiments (22-24). The artificial generation of mutant viruses in
214 laboratories and study of viral phenotypes by introducing mutations is called "reverse genetics", being a common
215 technique in virology. It has been claimed that SARS-CoV-2 must have been artificially generated because of
216 the unnatural presence of a codon (CGG) encoding a contiguous arginine at the furin cleavage site of SARS-
217 CoV-2. This claim has been refuted based on the following facts: 1) there is no logical reason for a genetically
218 engineered virus to utilize such a suboptimal furin cleavage site; 2) The only previous study on artificial insertion
219 of furin cleavage sites at the S1/S2 boundary of the S protein of SARS-CoV-1 using the pseudotype virus
220 experimental system utilized the optimal "RRSRR" sequence, which is different from the furin cleavage site's
221 sequence present in SARS-CoV-2; 3) There is no evidence of previous studies at the Wuhan Institute of Virology
222 that artificially inserted a complete furin cleavage site in coronaviruses; 4) Unnatural CGG codons adjacent to
223 arginine at the furin cleavage site are rare in coronaviruses but are observed at a particular frequency in SARS-
224 CoV-1, SARS-CoV-2, and other human coronaviruses. However, these are only declarations and are not logical.
225 No one has offered an explanation why a naturally occurring virus would utilize a suboptimal furin cleavage
226 site. There has been no mention of the technical possibility of inserting this furin cleavage site or a CGG codon
227 artificially. The insertion of a polybasic furin cleavage site into the S protein makes it impossible to conclude
228 whether SARS-CoV-2 is a naturally occurring or an artificial virus.

229 Despite the accumulation of many mutations in the S protein of Omicron mutants, most of the mutations are
230 non-synonymous, with only one synonymous mutation of c25000u, which is highly unnatural, leading to the
231 hypothesis that the Omicron mutants were artificially synthesized. The following results presented in this study
232 may support the hypothesis that the Omicron variants were artificially synthesized rather than naturally
233 occurring: 1) the presence of Omicron variant-associated isolates with one mutation site being the Wuhan-type;
234 2) the almost complete absence of synonymous mutations in the S protein in these isolates; 3) the Omicron
235 variant, which should have been first reported to WHO from South Africa on November 24, 2021, was already
236 endemic in Puerto Rico in 2020, and there were isolates that were recombinants between Omicron strains BA1
237 and BA2. In addition, the Omicron mutant-related isolates (BA.1-0.1, BA.1.1-0.1, and BA.2-0.1 isolates) with
238 a Wuhan-type mutation at one of the mutation sites were established. Some had synonymous mutations after

239 establishing the Omicron mutant-related isolates (Fig. 2 and Supplemental Figure 2 Synonymous Others). It is
240 reasonable to assume that viruses with the reversion amino acid mutations caused by non-synonymous mutations
241 in the S protein were artificially synthesized and then acquired further synonymous mutations in the natural
242 environment.

243 Assuming that artificially synthesized mutants with only non-synonymous mutations are spread globally, this
244 would explain how mutants with non-synonymous mutations without previous synonymous mutations develop
245 synonymous mutations under natural circumstances. Considering the current epidemic situation of SARS-CoV-
246 2, it is unlikely that these viruses arose spontaneously. Based on our efforts to explain the formation of the
247 SARS-CoV-2 isolates, they were formed by a completely new mechanism that cannot be explained by previous
248 biology.

249 One idea, the hypothesis that these viruses were artificially generated, is more reasonable than proposing a novel
250 mutation acquisition mechanism. However, is there any reason to artificially create these mutants, which are
251 unlikely to have occurred naturally, given the current SARS-CoV-2 epidemic?

252 It is known that the pathogenicity, host specificity, cell tropism, and immunogenicity of numerous viruses can
253 be altered by mutation of a single (or several) amino acid(s) of a viral protein on the viral envelope (envelope
254 protein, HA protein, spike protein, etc.). A single-amino-acid substitution in the HA protein of the 2009
255 pandemic A (H1N1) influenza viruses changed their replication and pathogenicity (25). In the Chikungunya
256 virus, single amino acid changes in the E2 glycoprotein influenced glycosaminoglycan utilization for target-cell
257 binding (26), and a single amino acid change in the E1 glycoprotein affected mosquito vector specificity and
258 epidemic potential (27). In previous coronaviruses such as MERS-CoV and SARS-CoV-1, point mutations have
259 been demonstrated to confer resistance to neutralizing antibodies (28-30).

260 Consider that the SARS-CoV-2 Omicron variant and its one-amino-acid reversion mutants were artificially and
261 systematically generated. In that case, we should suspect that the other variants (Alpha to Delta) were also
262 artificially generated viruses. Indeed, the lack of findings to date that many of the various mutations seen,
263 especially in the early variants, are indeed associated with increased viral infection (31) supports the hypothesis
264 that each variant was artificially synthesized to identify the amino acids of the S protein responsible for
265 infectivity and pathogenicity. The possibility that the set of mutants was artificially generated to identify amino
266 acids of the S protein involved in the infectivity and virulence is supported.

267 Reverse genetics experiments are an essential part of virus research, and it is inimical to virus research to
268 consider that artificially synthesized viruses were deliberately spread throughout the world. However, now that
269 reverse genetics has become common in virus research, we believe it is not scientific to discuss the mutation
270 process of SARS-CoV-2 without excluding the possibility of artificially synthesized viruses.

271 Finally, we would like to add that while artificially synthesized viruses may have spread, we are not criticizing
272 reverse genetics technology, as such technology has led to marked advances in virology. In addition, our analysis
273 employed databases with a limited number of viral sequences, and we cannot deny the possibility that unreliable
274 data may have been registered due to technical problems in sequencing or some other issues. Furthermore, we
275 do not conclude that these viruses were artificially synthesized and distributed based on malicious intent. This
276 study aims to point out that SARS-CoV-2 has undergone unthinkable mutations based on conventional
277 coronavirus mutation mechanisms, and we hope that the possibility of artificial creation is included in serious
278 discussions on the formation of SARS-CoV-2 variants.

279 Nonetheless, the analysis we have shown here concludes that the Omicron variants were formed by a completely
280 new mechanism that cannot be explained by previous biology. The process of how SARS-CoV-2 mutations
281 occurred should prompt a reconsideration of the SARS-CoV-2 pandemic. If the SARS-CoV-2 epidemic strain
282 is an artificially mutated virus and if the corona disaster (corona hoopla) was a well-designed global experiment
283 in human inoculation and a social experiment, then the design of this experiment and the nature of the virus used
284 make it likely that this experiment (corona hoopla) is a preliminary experiment.

285 4 **Methods**

286 4. 1 **Data acquisition**

287 The SARS-CoV-2 RNA genome, genes, and proteins according to an annotation of SARS-CoV-2 Wuhan-Hu-
288 H1 (COVID-19/Wuhan-Hu-1CHN/2019/First Isolate) NCBI Reference Sequence: NC_045512.2 were used as
289 references for the definition of mutations, and provided a basis for the numbering of nucleotides and amino acids
290 of each protein. Genome data of SARS-CoV-2 isolates described in this article were obtained from the NCBI
291 Nucleotide database (<https://www.ncbi.nlm.nih.gov/>) on 25/11/2022 to 17/03/2023.

292 4. 2 **Query of representative SARS-CoV-2 variant genome**

293 Amino acid sequences of spike protein of SARS-CoV-2 variants (Alpha:B.1.1.7, Beta:B.1.351, Gamma:P1,
294 Delta:B.1.617.2.63, Lambda:C.37, Mu:B.1.621, Omicron:BA.1, BA.1.1, and BA.2) were obtained from an
295 Internet site, Stanford Coronavirus Antiviral & Resistance Database (<https://covdb.stanford.edu/>) or Covariant
296 (<https://covariants.org/>), and used as a query sequence for an NCBI protein BLAST search (blastp: protein-
297 protein BLAST,
298 https://blast.ncbi.nlm.nih.gov/Blast.cgi?PROGRAM=blastp&PAGE_TYPE=BlastSearch&LINK_LOC=blasthome). Then, the whole genome sequence of each isolate bearing the query spike sequence was derived from the
299 BLAST search result, identified with query amino acid sequences of 100%. The nucleotide sequences of the
300 detected SARS-CoV-2 genome were as follows: GenBank Accession No.: GenBank: MW423686.2;
301 MW430966.1; MW430967.1; MW422256.1; MW598419.1; MW667552.1; MW667553.1; MW721502.1;
302 MW721504.1; MW520923.1; MW642248.1; MW642249.1; MW642250.1; MZ182066.1; MZ155303.1;
303 MZ155230.1; MZ170364.1; MZ179869.1; MW666666.1; MW696612.1; MW699217.1; MW644498.1;
304 MZ727706.1; MZ620161.1; MZ637380.1; MZ637401.1; MZ780550.1; OL672836.1; OL677199.1;
305 OP769083.1; OL764360.1; OL815447.1; ON762438.1; OL849989.1; OL897126.1; OL896945.1;
306 OL896936.1; OL896931.1; OM233931.1; OM072551.1; OM072822.1; OM296922.1.
307
308

309 4. 3 **Query of SARS-CoV-2 Omicron variant genome bearing an S protein amino acid sequence in**
310 **which one of the Omicron-type nucleotide mutation subsets was not mutated and retains the original**
311 **SARS-CoV-2 Wuhan-Hu-H1-type arrangement.**

312 For each of the Omicron variants, BA.1, BA.1.1, and BA.2, the isolate series bearing an S protein amino acid
313 sequence in which one of the Omicron-type nucleotide mutation subsets is not mutated and retains the original
314 SARS-CoV-2 Wuhan-Hu-H1-type arrangement were named BA.1-0.1, BA.1.1-0.1 and BA.2-0.1, respectively.
315 In addition, in this article, we named the amino acid sequences of spike protein of BA.1, BA.1.1, and BA.2 as
316 BA.1_S, BA.1.1_S, and BA.2_S, respectively, and then the series of amino acid sequences of spike protein of
317 BA.1-0.1, BA.1.1-0.1, and BA.2-0.1 were named, respectively, as follows: Omicron BA.1-0.1 spike series
318 (BA.1-0.1_Ss) were named as BA.1_S:V67A; BA.1_S:69H_70V; BA.1_S:I95T;
319 BA.1_S:D142G_143V_144Y_145Y; BA.1_S:I211N_212L; BA.1_S:ΔEPE; BA.1_S:D339G; BA.1_S:L371S;
320 BA.1_S:P373S; BA.1_S:F375S; BA.1_S:N417K; BA.1_S:K440N; BA.1_S:S446G; BA.1_S:N477S;
321 BA.1_S:K478T; BA.1_S:A484E; BA.1_S:R493Q; BA.1_S:S496G; BA.1_S:R498Q; BA.1_S:Y501N;
322 BA.1_S:H505Y; BA.1_S:K547T; BA.1_S:G614D; BA.1_S:Y655H; BA.1_S:K679N; BA.1_S:H681P;
323 BA.1_S:K764N; BA.1_S:Y796D; BA.1_S:K856N; BA.1_S:H954Q; BA.1_S:K969N and BA.1_S:F981L /
324 Omicron BA.1.1-0.1 spike series (BA.1.1-0.1_Ss) were named as BA.1.1_S:V67A; BA.1.1_S:69H_70V;
325 BA.1.1_S:I95T; BA.1.1_S:D142G_143V_144Y_145Y; BA.1.1_S:I211N_212L; BA.1.1_S:ΔEPE;
326 BA.1.1_S:D339G; BA.1.1_S:L371S; BA.1.1_S:P373S; BA.1.1_S:F375S; BA.1.1_S:N417K;
327 BA.1.1_S:K440N; BA.1.1_S:S446G; BA.1.1_S:N477S; BA.1.1_S:K478T; BA.1.1_S:A484E;
328 BA.1.1_S:R493Q; BA.1.1_S:S496G; BA.1.1_S:R498Q; BA.1.1_S:Y501N; BA.1.1_S:H505Y;
329 BA.1.1_S:K547T; BA.1.1_S:G614D; BA.1.1_S:Y655H; BA.1.1_S:K679N; BA.1.1_S:H681P;
330 BA.1.1_S:K764N; BA.1.1_S:Y796D; BA.1.1_S:K856N; BA.1.1_S:H954Q; BA.1.1_S:K969N;
331 BA.1.1_S:F981L / Omicron BA.2-0.1 spike series (BA.2-0.1_Ss) were named as BA.2_S:I19T;

332 BA.2_S:24L_25P_26P_S27A; BA.2_S:D142G; BA.2_S:V213G; BA.2_S:D339G; BA.2_S:F371S;
333 BA.2_S:P373S; BA.2_S:F375S; BA.2_S:A376T; BA.2_S:N405D; BA.2_S:S408R; BA.2_S:N417K;
334 BA.2_S:K440N; BA.2_S:N477S; BA.2_S:K478T; BA.2_S:A484E; BA.2_S:R493Q; BA.2_S:R498Q;
335 BA.2_S:Y501N; BA.2_S:H505Y; BA.2_S:G614D; BA.2_S:Y655H; BA.2_S:K679N; BA.2_S:H681P;
336 BA.2_S:K764N; BA.2_S:Y796D; BA.2_S:H954Q; BA.2_S:K969N, and these constructs are shown in Figs. 2,
337 4 and supplemental Figure 1. These amino acids sequences of spike protein of SARS-CoV-2 Omicron variants,
338 BA.1-0.1, BA.1.1-0.1, and BA.2-0.1, were used as query sequences for an NCBI protein BLAST search. Then,
339 the whole genome sequences of BA.1-0.1, BA.1.1-0.1, and BA.2-0.1 isolates bearing the query spike sequence
340 were derived from the BLAST search results, identified with a query amino acid sequence of 100%. The
341 nucleotide sequences of the detected SARS-CoV-2 genome were as follows: GenBank Accession No.:
342 OM117411.1; OP797378.1; OM789835.1; OP928789.1; OP928803.1; OP929381.1; OP929396.1;
343 OP929417.1; OM173977.1; OM518459.1; OM566981.1; ON019560.1; OM097227.1; OM096937.1;
344 OM099902.1; OM117114.1; OM096685.1; OM354436.1; OM646886.1; OM472901.1; OM364511.1;
345 OM131858.1; OL815451.1; OL896986.1; OL897116.1; OL897118.1; OL896964.1; OM367679.1;
346 OM343778.1; OM409228.1; OM396816.1; OM134162.1; OM075886.1; OM123427.1; OM122677.1;
347 OM121681.1; OM224850.1; ON246090.1; OM931599.1; OM864873.1; OM906519.1; OM906587.1;
348 OM464776.1; OM015999.1; OM015958.1; OM015597.1; OM016329.1; OL898806.1; OL898861.1;
349 OM016937.1; OM016186.1; OM036549.1; OM051171.1; OM126493.1; OM079115.1; OM099199.1;
350 OM134489.1; OM098796.1; ON618279.1; ON618009.1; OM627701.1; OM356511.1; OM295457.1;
351 ON700063.1; OM033824.1; ON368355.1; OM084700.1; ON208126.1; OM566593.1; OM945690.2;
352 ON030252.1; ON019844.1; OM890075.1; ON020044.1; OM833954.1; ON376082.1; OM084604.1;
353 OP795273.1; ON066609.1; OM352882.1; OM290510.1; OM369978.1; OM199342.1; OM011974.1;
354 OM090274.1; OM043984.1; OM121683.1; OM121624.1; OM175506.1; OM360429.1; OM360221.1;
355 OM358058.1; OM500517.1; OM135027.1; OM742858.1; OM521685.1; OM896558.1; ON694155.1;
356 OM686755.1; OM484260.1; OM332056.1; OM156397.1; OM079447.1; OM134645.1; OM173298.1;
357 OM123082.1; OM116023.1; OM652943.1; OL994299.1; OL994920.1; OM122027.1; OM121015.1;
358 OL898817.1; OM527504.1; OM225320.1; OM931491.1; OM931575.1; OM931587.1; OM034409.1;
359 OM036283.1; OL996129.1; OM035680.1; OM096996.1; ON065532.1; OM968098.1; OM816604.1;
360 ON235452.1; ON334146.1; OP024162.1; OP209732.1; OM354578.1; OM099080.1; OM297301.1;
361 OM297438.1; OM365368.1; OM449159.1; OM078863.1; OM096959.1; OM117155.1; OM133880.1;
362 OM077358.1; OM372005.1; OM770362.1; OM897488.1; OM918459.1; OM918478.1; OL897115.1;
363 OL897114.1; OL986779.1; OL986696.1; OL987046.1; ON831866.1; OM864099.1; OM863888.1;
364 OP745925.1; ON831672.1; OM043643.1; OM176192.1; OM226685.1; OM343689.1; OM295527.1;
365 OM894975.1; OM846676.1; OM822024.1; OM846844.1; OM906550.1; OM015933.1; OM016323.1;
366 OM016331.1; OM035685.1; OM022498.1; OM156115.1; OM036875.1; OM099560.1; OM199246.1;
367 OM067048.1; OM079299.1; OM099911.1; OM116588.1; OM097010.1; OM173300.1; OM805961.1;
368 OM983266.1; OM983325.1; ON618010.1; OM084691.1; ON021265.1; ON039239.1; ON056981.1;
369 ON144127.1; OM770527.1; OM156164.1; OM155119.1; OM199353.1; OM084630.1; OM084605.1;
370 OM084621.1; OM359369.1; OM411574.1; OM584789.1; OM720486.1; OM429777.1; ON047062.1;
371 ON065416.1; OP415118.1; OM954373.1; ON042406.1; OM335528.1; OM332335.1; OM353626.1;
372 OM332813.1; OM197398.1; OM226919.1; OM228399.1; OM225859.1; OM271353.1; OM159454.1;
373 OM224473.1; OM358278.1; OM361030.1; OM412141.1; OM496298.1; OM044048.1; OM121864.1;
374 OM224477.1; OM227379.1; OM228453.1; OM622156.1; OM906370.1; OM970683.1; ON117965.1;
375 OM198667.1; OM357800.1; OM357161.1; OM335230.1; OM261124.1; OM077578.1; OM497172.1;
376 OM625194.1; OM907131.1; ON047464.1; OM911851.1; OM042846.1; OM155337.1; OM097339.1;
377 OM116805.1; OM134409.1; OM686782.1; OM695863.1; OM724725.1; OM174366.1; OM822132.1;
378 OM822106.1; OM822105.1; OM822485.1; OM135143.1; OM125829.1; OM098855.1; OM156118.1;
379 OM155114.1; OM863926.1; OP359104.1; ON209298.1; ON232806.1; ON421981.1; ON811217.1;
380 OM698275.1; ON052769.1; ON060006.1; ON060007.1; ON060009.1; OM843171.1; OM843276.1;
381 OM843550.1; OM843316.1; OM843340.1; ON049267.1; ON450720.1; ON250163.1; ON256603.1;
382 ON480422.1; OM888844.1; OM890089.1; ON009425.2; ON082904.1; OM901275.1; OM877094.2;
383 OM877095.2; OM877096.2; OM877097.2; ON378542.1; ON389858.1; ON389889.1; ON390359.1;
384 OM936703.1; ON352711.1; ON378000.1; ON177702.1; ON205494.1; ON378633.1; ON617689.1;

385 ON619375.1; OM567618.1; OM659585.1; OM770913.1; OM781641.1; OM533441.1; OM533458.1;
386 OM570235.1; OM570252.1; OM570249.1; OM283361.1; OM283362.1; OM283320.1; OM283343.1;
387 ON618014.1; ON618018.1; ON618019.1; ON618363.1; ON311615.1; ON383919.1; OP579158.1;
388 OP054411.1; ON633107.1; ON414693.1; ON422887.1; OP364296.1; OP629673.1; ON363097.1;
389 OP633561.1; ON458445.1; ON592247.1; ON549687.1; ON067040.1; ON321116.1; ON199452.1;
390 ON200331.1; OM861064.1; OM969592.1; ON019120.1; ON221861.1; OM861619.1; ON091288.1;
391 ON151370.1; ON233850.1; ON236456.1; ON296711.1; ON535443.1; ON624524.1; ON377450.1;
392 ON397268.1; ON239032.1; ON373649.1; ON481637.1; ON701163.1; ON312677.1; ON349263.1;
393 ON377487.1; ON377609.1; OM638574.1; OM911616.1; OM988767.1; ON019770.1; OM988769.1;
394 ON468158.1; ON608924.1; ON604965.1; ON535763.1; ON378227.1; ON378238.1; ON728470.1.

395 4. 4 Query of recombinant SARS-CoV-2 Omicron variant between BA.1 and BA.2 genome

396 Deduced recombinant spike protein between Omicron variants, BA.1 and BA.2 shown as BA.1_S:T19I_L24-
397 _P25-_P26-_A27S_V213G_S371F_T376A_D405N_R408S was used as a query sequence for an NCBI
398 protein BLAST search. The whole genome sequence of BA.1 and BA.2 recombinant-Omicron isolates showed
399 some of the specific amino acid mutations observed in variant BA.1 and BA.2 in the S protein. The nucleotide
400 sequences of the detected SARS-CoV-2 genome were as follows: GenBank Accession No.: OM360636.1;
401 OM410816.1; OM429902.1; OM497964.1; OM565587.1; OM628132.1; ON549899.1; ON449685.1;
402 ON176765.1; OM628094.1; ON099844.1; OM942313.1; ON395480.1; ON171854.1; ON172005.1;
403 ON076710.1; ON928946.1; OM932113.1; OM942438.1; OM989528.1; OM499181.1; ON414822.1;
404 OM878325.1; ON103067.1; ON103153.1; ON419036.1; ON928719.1; ON337887.1; ON420444.1;
405 ON146520.1; OM469541.1; OM904085.1; ON254531.1; OM881098.1; ON373310.1.

406 4. 5 Query of SARS-CoV-2 Omicron variant genome detected in Puerto Rico in 2020

407 Nucleotide sequences were searched using the keywords PRI PR-UPRRP 2020 (Search details: PRI[All
408 Fields] AND (PR[All Fields] AND UPRRP[All Fields]) AND 2020[All Fields]). The search results were all
409 SARS-CoV-2 isolate genome sequences. Among these sequences, SARS-CoV-2 Omicron variant-related
410 sequences were picked up as follows: GenBank Accession No.: ON928761.1; ON928660.1; ON928794.1;
411 ON928762.1; ON928848.1; ON928741.1; ON928918.1; ON928680.1; ON928975.1; ON928949.1;
412 ON928673.1; ON928865.1; ON928716.1; ON928663.1; ON928779.1; ON928896.1; ON928946.1;
413 ON928912.1; ON928704.1; ON928873.1; ON928813.1; ON928898.1; ON928765.1; ON928912.1;
414 ON928883.1; ON928957.1; ON928880.1; ON928699.1; ON928724.1; ON928941.1.

415 Genomes were aligned using SnapGene software or GENETYX software. Numbering of nucleotides and
416 amino acids of each protein was determined using Wuhan-Hu-1 (NC_045512.2; COVID-19/Wuhan-Hu-
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529

530 **Conflict of Interest**

531 The authors declare that the research was conducted in the absence of any commercial or financial
532 relationships that could be construed as a potential conflict of interest.

533 **Figure legends**

534 **Fig. 1. Mutation subsets of S protein of SARS-CoV-2 variants.**

535 Sequences of S protein of SARS-CoV-2 variants (variants of concern, VOCs: Alpha:B.1.1.7, Beta:B.1.351,
536 Gamma:P1, Delta:B.1.617.2.63, and Omicron:BA.1; BA.2 and variants of interest, VOIs: Lambda:C.37,
537 Mu:B.1.621) are compared with the SARS-CoV-2 Wuhan-Hu-H1 reference sequence, and different amino acids
538 (amino acid change, deletion, and insertion) and synonymous changes of nucleotides are shown. Non-
539 synonymous changes are shown by amino acid changes (capital letters), and synonymous changes are shown by
540 nucleotide changes (small letters). Amino acids different from Wuhan-Hu-H1 found in each variant: Alpha:
541 B.1.1.7, Beta: B.1.351, Gamma: P1, Delta: B.1.617.2.63, Lambda: C.37, Mu: B.1.621, and Omicron: BA.1,
542 BA.2 are highlighted with red, orange, green, yellow, aquamarine, lime, deep sky blue, and blue violet,
543 respectively. Amino acid changes common to Omicron: BA.1 and BA.2 are shown in purple.

544

545 **Fig. 2. Mutations of S proteins of SARS-CoV-2 Omicron isolates.**

546 **(A)** Different amino acids and synonymous changes of nucleotides in S proteins of SARS-CoV-2 Omicron BA.1,
547 BA.1.1 isolates, and BA.1-0.1s compared with SARS-CoV-2 Wuhan-Hu-H1. Nucleotide deletions and
548 insertions were "deletion¹" (deletion: nt 21,766-21,771), "deletion²" (deletion: nt 21,987-21,995), "deletion³"
549 (deletion: nt 22,194-22,196), and "insertion⁴" (insertion between 22,206-22,196), and introduced amino acid
550 changes were H69_V70-, G142D_V143_Y144_Y145-, N211I_L212-, and 215ins.EPE, respectively. **(B)**
551 Different amino acids and synonymous nucleotide changes in S proteins of SARS-CoV-2 Omicron BA.1.1-0.1
552 isolates. Amino acids different from Wuhan-Hu-H1 found in each variant: Alpha: B.1.1.7, Beta: B.1.351,
553 Gamma: P1, Delta: B.1.617.2.63, Mu: B.1.621, and Omicron: BA.1, BA.2 are highlighted with red, orange,
554 green, yellow, lime, deep sky blue, and blue violet, respectively. Amino acid changes common to Omicron:BA.1
555 and BA.2 are highlighted with purple.

556

557 **Fig. 3. Estimated homologous recombination breakpoints of the SARS-CoV-2 S gene of Omicron BA.1-**
558 **0.1 or BA.1.1-0.1.**

559 Sequence alignment of amino acids and their coding nucleotides (nt.21,746-21,787; nt.22,658-22,702;
560 nt.22,976-23,011, and nt.23,582-23,620) containing the mutation point of the SARS-CoV-2 S gene of the
561 Omicron BA.1 variant compared with SARS-CoV-2 Wuhan-Hu-H1. Changed nucleotides and amino acids of
562 Omicron BA.1 are shown in red letters. Estimated homologous recombination breakpoints of the SARS-CoV-
563 2 S gene of Omicron BA.1-0.1 or BA.1.1-0.1 are shown by asterisks.

564

565 **Fig. 4. Representative mutations of SARS-CoV-2 Omicron isolates other than S protein.**

566 **(A)** Representative amino acids and synonymous changes of nucleotides of SARS-CoV-2 Omicron BA.1,
567 BA.1.1 isolates, and BA.1-0.1 compared with SARS-CoV-2 Wuhan-Hu-H1. **(B)** Representative amino acids
568 and synonymous changes of nucleotides of SARS-CoV-2 Omicron BA.1.1-0.1 compared with SARS-CoV-2
569 Wuhan-Hu-H1. Amino acids different from Wuhan-Hu-H1 found in each variant: Alpha: B.1.1.7, Lambda: C.37,
570 Mu: B.1.621, and Omicron: BA.1 are highlighted with red, aquamarine, deep sky blue, and blue violet,
571 respectively.

572 Amino acid changes common to Omicron: BA.1 and BA.2 are shown in purple. Synonymous nucleotide
573 changes: c2470u observed in Omicron:BA.1.1 mainly shown with blue. Synonymous and non-synonymous
574 changes: u10135c of nsp5, L106F in ORF3, and D343G in N protein subset observed in ~40% of Omicron;

575 BA.1-0.1 are highlighted with emerald-green. Undetermined nucleotides or amino acids are shown as UD or X,
576 respectively.

577

578 **Fig. 5. Mutations of S proteins of SARS-CoV-2 Omicron BA.1-BA.2 recombinant isolates and SARS-CoV-2 Omicron BA.1 and BA.2 isolates detected in Puerto Rico in 2020.**

580 (A) Different amino acids and synonymous change of nucleotides in S proteins of SARS-CoV-2 Omicron BA.1-
581 BA.2 recombinant isolates compared with SARS-CoV-2 Wuhan-Hu-H1. Nucleotide deletions, "deletion⁵"
582 (deletion: nt 21,633-21,641), introduced the amino acids changes L24- P25- P26- A27S. (B) Different amino
583 acids and synonymous change of nucleotides in S proteins of SARS-CoV-2 Omicron BA.1.1 and Omicron
584 BA.1-BA.2 recombinant isolate, highlighted with magenta (GenBank: ON928946.1), Omicron BA.2, and
585 Omicron 2-0.1(K440N), detected in Puerto Rico in 2020. Amino acids different from Wuhan-Hu-H1 found in
586 each variant: Alpha: B.1.1.7, Beta: B.1.351, Gamma: P1, Delta: B.1.617.2.63, Mu: B.1.621, and Omicron: BA.1,
587 BA.2 are highlighted with red, orange, green, yellow, lime, deep sky blue, and blue-violet, respectively. Amino
588 acid changes common to Omicron: BA.1 and BA.2 are highlighted with purple.

589

590 **Supplemental Figure 1**

591 **Human coronavirus 229E strains detected in Seattle, USA, in 2015 and 2019.**

592 Alignment of nucleotide (A) and amino acid (B) sequences of the S protein of Human coronavirus 229E strains,
593 HCoV_229E/Seattle/USA/SC3112/2015 (GenBank: KY983587.1), and CoV_229E/Seattle/USA/SC0865/2019
594 (GenBank: MN306046.1). The number of nucleotide substitutions observed between them was 32, amino acid
595 substitutions numbered 18 between them, and the synonymous (14: 32-18)-non-synonymous mutation (18) rate
596 between them was 1.285

597

598 **Supplemental Figure 2**

599 **Different amino acids and synonymous changes of nucleotides in S proteins of SARS-CoV-2 Omicron**
600 **BA.2 isolates and BA.2-0.1s compared with SARS-CoV-2 Wuhan-Hu-H1.**

601 Nucleotide deletions, "deletion⁵" (deletion: nt 21,633-21,641), introduced the amino acid changes L24- P25-
602 P26- A27S. Amino acids different from Wuhan-Hu-H1 found in each variant: Alpha: B.1.1.7, Beta: B.1.351,
603 Gamma: P1, Delta: B.1.617.2.63, Mu: B.1.621, and Omicron: BA.1, BA.2 are highlighted with red, orange,
604 green, yellow, lime, deep sky blue, and blue-violet, respectively. Amino acid changes common to Omicron:
605 BA.1 and BA.2 are highlighted with purple.

606

607 **Supplemental Figure 3**

608 **Estimated homologous recombination breakpoints of the SARS-CoV-2 S gene of the Omicron BA.2-0.1**
609 **or BA.1-BA.2 recombinant.**

610 (A) Sequence alignment of the amino acids and coding nucleotides (nt. 22,658-22,702) containing the mutation
611 point of the SARS-CoV-2 S gene of Omicron BA.2 variants compared with SARS-CoV-2 Wuhan-Hu-H1. (B)
612 Sequence alignment of the amino acids and coding nucleotides (nt. 22,178-22,222) containing the mutation point
613 of the SARS-CoV-2 S gene of Omicron BA.1, BA.2 variant and BA.1-BA.2 recombinant isolate compared with
614 SARS-CoV-2 Wuhan-Hu-H1. Changed nucleotides and amino acids of Omicron variants BA.1, BA.2, and

615 BA.1-BA.2 recombinant isolates compared with SARS-CoV-2 Wuhan-Hu-H1 sequences are shown in red
616 letters. Asterisks show an estimated homologous recombination breakpoint of the SARS-CoV-2 S gene of
617 Omicron BA.2-0.1.

Fig. 3

21, 750 21, 760 21, 770 21, 780
 SARS-CoV-2_Wuhan-Hu-1 GUUACUUGGUUCCAUGCUAUACAUGUCUCUGGGACCAAUGGU
 SARS-CoV-2_Omicron_BA. 1 GUUACUUGGUUCCAUGUUAU-----CUCUGGGACCAAUGGU
 break point ***
 V U W F H A I H V S G U N G
 V U W F H V I - - S G U N G
 A67V H69- V70-

22, 660 22, 670 22, 680 22, 690 22, 700
 UCUGUCCUAUAUAAUCCGCAUCAUUUCCACUUUUAAGUGUUAU
 UCUGUCCUAUAUAAUCUCGCACCAUUUUCACUUUUAAGUGUUAU

 S V L Y N S A S F S T F K C Y
 S V L Y N L A P F F T F K C Y
 S371L S373P S375F

22, 980 22, 990 23, 000 23, 010
 AUCUAUCAGGCCGGUAGCACACCUUGUAAUGGUGUU
 AUCUAUCAGGCCGGUAACAACCUUGUAAUGGUGUU
 **
 I Y Q A G S T P C N G V
 I Y Q A G N K P C N G V
 S477N T478K

23, 590 23, 600 23, 610 23, 620
 UAUCAGACUCAGACUAAUUCUCCUCGGCGGGCACGUAGU
 UAUCAGACUCAGACUAGUCUCUAUCGGCGGGCACGUAGU

 Y Q T Q T N S P R R A R S
 Y Q T Q T K S H R R A R S
 N679K P681H

Supplemental Figure 1

A

HCoV-229E_Seattle_USA_S3112_2015_seq 1 ATGTTGTTTTACTGTGTCATATGCTTGGTATGATTCGGTGTGCAACCTAAAT
HCoV-229E_Seattle_USA_S3112_2015_seq 2 ATGTTGTTTTACTGTGTCATATGCTTGGTATGATTCGGTGTGCAACCTAAAT
HCoV-229E_Seattle_USA_S3112_2015_seq 61 GGAGCAACACTAGTCACTCTTGGCAAGCCGCTGTTGCTCCGGAAAGATGATTT
HCoV-229E_Seattle_USA_S3112_2015_seq 62 GGAGCAACACTAGTCACTCTTGGCAAGCCGCTGTTGCTCCGGAAAGATGATTT
HCoV-229E_Seattle_USA_S3112_2015_seq 121 CGTGTGGAGTGGTGGTATATACCTCCCMCTTCAATTAATATTGGTCTGCTCTA
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HCoV-229E_Seattle_USA_S3112_2015_seq 1501 TTAAAGATCTACTAGTGGCAATCTACTGCTACTGCTACTGCTACTGCTACTGCT
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HCoV-229E_Seattle_USA_S3112_2015_seq 1561 CTTGTTGTTAATATACAGTGGCAATTTTAACTAAAGAGCTGCTGTGTT
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HCoV-229E_Seattle_USA_S3112_2015_seq 1741 GCTGTCACACAGTATCTTATGATGATGATGATGATGATGATGATGATGATGATGAT

B

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HCoV-229E_Seattle_USA_S3112_2015_seq 2760 TTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 2761 TTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 2820 AAGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 2821 AAGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 2880 GAGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 2881 GAGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 2940 TGGTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 2941 TGGTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 3060 CTTACATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 3061 CTTACATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 3120 GCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 3121 GCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 3180 TTAGTATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 3181 TTAGTATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 3240 ACTATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
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HCoV-229E_Seattle_USA_S3112_2015_seq 3300 TACTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 3301 TACTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 3360 AAGTGGCTCAAGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 3361 AAGTGGCTCAAGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 3420 TCACTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
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HCoV-229E_Seattle_USA_S3112_2015_seq 3480 TCGGCTCTTTAGTGTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 3481 TCGGCTCTTTAGTGTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 3516 CTTATACAGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT
HCoV-229E_Seattle_USA_S3112_2015_seq 3517 CTTATACAGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT

HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 1 MFVLLVAYALHIAAGCTTNGTNTSHVNCVCGHSENFVAFSGVYIPSNFANNFLL
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 2 MFVLLVAYALHIAAGCTTNGTNTSHVNCVCGHSENFVAFSGVYIPSNFANNFLL
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 61 NNTSSVVDGVRFPQLLNLCLVSSQFRTGFVYFNGTRGRACKGFFYSNASDVIYRN
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 62 NNTSSVVDGVRFPQLLNLCLVSSQFRTGFVYFNGTRGRACKGFFYSNASDVIYRN
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 121 INFENLRRTGLTKTYSKAVFYFNTNLTLSGDMHPSGTVLGNFYFVNTTIGNETTS
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 122 INFENLRRTGLTKTYSKAVFYFNTNLTLSGDMHPSGTVLGNFYFVNTTIGNETTS
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 180 AVFGLPKTVRFVRSRTHFYNGYRFLSLGAEVNFVNTAATVCTVALASYADVL
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 181 AVFGLPKTVRFVRSRTHFYNGYRFLSLGAEVNFVNTAATVCTVALASYADVL
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 240 VWSQTAIANITVNSVNLRCQSLFSDPDGFYSTSPQVPLVMSVLSVLYPHKHTF
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 241 VWSQTAIANITVNSVNLRCQSLFSDPDGFYSTSPQVPLVMSVLSVLYPHKHTF
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 300 TVLHVFQHRQPGKCYNCRPSVINTILANFNETKPLCVDSHFHTFQVNNKLRWSA
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 301 TVLHVFQHRQPGKCYNCRPSVINTILANFNETKPLCVDSHFHTFQVNNKLRWSA
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 360 STIDGNCPSFGKVFVFKVGSVCSLQKIPGGCAMPIMANLVKHSNIGSLVYSWSQD
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 361 STIDGNCPSFGKVFVFKVGSVCSLQKIPGGCAMPIMANLVKHSNIGSLVYSWSQD
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 420 DVTGVPKPKVEVSSFMVNLKCTKYNIDVSGGVIRISNDTFLNGTLYTSTSNLGL
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 421 DVTGVPKPKVEVSSFMVNLKCTKYNIDVSGGVIRISNDTFLNGTLYTSTSNLGL
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 480 FKVDTNGTYSITPCNPQQLVYQAVGMLSENFYSYGFVSNVEMPKFFYASNGTYN
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 481 FKVDTNGTYSITPCNPQQLVYQAVGMLSENFYSYGFVSNVEMPKFFYASNGTYN
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 540 CTDALVYSSFGVADGSIQVAPRNSYDVSVAIVLANSPISNWTISVQVEQLTST
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 541 CTDALVYSSFGVADGSIQVAPRNSYDVSVAIVLANSPISNWTISVQVEQLTST
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 600 PIVDCSTYVCGNRCVELLKYQTSACKTIEDALRNSAMLESADVSEMLTFDKKAFTLA
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 601 PIVDCSTYVCGNRCVELLKYQTSACKTIEDALRNSAMLESADVSEMLTFDKKAFTLA
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 660 NYSSFQDNLSSVPLSPRSGRVAGSAEDELFSKLVTSGLGTVDADYKCKTKGLSIA
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 661 NYSSFQDNLSSVPLSPRSGRVAGSAEDELFSKLVTSGLGTVDADYKCKTKGLSIA
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 720 DLACAYQYNGIMVLPQDAERAEMMYTGSLLGGALGLLTAASIFPFLSLQSLRNYVAL
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 721 DLACAYQYNGIMVLPQDAERAEMMYTGSLLGGALGLLTAASIFPFLSLQSLRNYVAL
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 780 QTDVLEQENQLLAASFNMKTNDVDFGQNDALDTQSQAQVATALNKIQDQVNNQGN
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 781 QTDVLEQENQLLAASFNMKTNDVDFGQNDALDTQSQAQVATALNKIQDQVNNQGN
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 840 SLNHLTSQLRNFQAISSSQIAYRDLIIQADQVORLITGRLLANVFSHTLTKYTE
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 841 SLNHLTSQLRNFQAISSSQIAYRDLIIQADQVORLITGRLLANVFSHTLTKYTE
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 900 VRASRLAQQVNECVSKSRKRYFGCNGHTFSLVNAPEGLVFLHTLPTQYKQVEA
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 901 VRASRLAQQVNECVSKSRKRYFGCNGHTFSLVNAPEGLVFLHTLPTQYKQVEA
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 960 WSLGCVQDINGVLRQPLNLKYEQNYRISIRMEFPIRPIADPQVLENCVTFVNISS
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 961 WSLGCVQDINGVLRQPLNLKYEQNYRISIRMEFPIRPIADPQVLENCVTFVNISS
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 1020 RSELQTLVPEYDWNKTLQELSKYLPNTVDPVLEQNYLNLSESTLEMSKALEN
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 1021 RSELQTLVPEYDWNKTLQELSKYLPNTVDPVLEQNYLNLSESTLEMSKALEN
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 1080 TVYQKQLTLDINSTLVDLKNWLNRYEKXNFWVQVQVLSVLLCCSSTGCG
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 1081 TVYQKQLTLDINSTLVDLKNWLNRYEKXNFWVQVQVLSVLLCCSSTGCG
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 1140 GFFSFCASSIIGCCSTCLPYVDKEKHQ
HCoV-229E_Seattle_USA_S3112_2015_Spike_seq 1141 GFFSFCASSIIGCCSTCLPYVDKEKHQ

Supplemental Figure 2

Variant	Definition	GenBank Accession No.	deletion																						Non-synonymous											Synonymous																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																											
			T19I	L24-	P25-	P26-	A27S	G142D	V213G	G339D	S371F	S373P	S375F	T376A	D405N	R408S	K417N	N440K	S477N	T478K	E484A	Q493R	Q498R	N501Y	Y505H	D614G	H655Y	N679K	P681H	N764K	D786Y	Q954H	N969K	c27292u*	c2500u*	Others*																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																											
BA.2	LARS-CoV-2 human, USA, CA-CDC-FG-20201-2021	GenBank:OM623001.1	Y518	Y524	Y525	Y526	Y527	Y528	Y529	Y530	Y531	Y532	Y533	Y534	Y535	Y536	Y537	Y538	Y539	Y540	Y541	Y542	Y543	Y544	Y545	Y546	Y547	Y548	Y549	Y550	Y551	Y552	Y553	Y554	Y555	Y556	Y557	Y558	Y559	Y560	Y561	Y562	Y563	Y564	Y565	Y566	Y567	Y568	Y569	Y570	Y571	Y572	Y573	Y574	Y575	Y576	Y577	Y578	Y579	Y580	Y581	Y582	Y583	Y584	Y585	Y586	Y587	Y588	Y589	Y590	Y591	Y592	Y593	Y594	Y595	Y596	Y597	Y598	Y599	Y600	Y601	Y602	Y603	Y604	Y605	Y606	Y607	Y608	Y609	Y610	Y611	Y612	Y613	Y614	Y615	Y616	Y617	Y618	Y619	Y620	Y621	Y622	Y623	Y624	Y625	Y626	Y627	Y628	Y629	Y630	Y631	Y632	Y633	Y634	Y635	Y636	Y637	Y638	Y639	Y640	Y641	Y642	Y643	Y644	Y645	Y646	Y647	Y648	Y649	Y650	Y651	Y652	Y653	Y654	Y655	Y656	Y657	Y658	Y659	Y660	Y661	Y662	Y663	Y664	Y665	Y666	Y667	Y668	Y669	Y670	Y671	Y672	Y673	Y674	Y675	Y676	Y677	Y678	Y679	Y680	Y681	Y682	Y683	Y684	Y685	Y686	Y687	Y688	Y689	Y690	Y691	Y692	Y693	Y694	Y695	Y696	Y697	Y698	Y699	Y700	Y701	Y702	Y703	Y704	Y705	Y706	Y707	Y708	Y709	Y710	Y711	Y712	Y713	Y714	Y715	Y716	Y717	Y718	Y719	Y720	Y721	Y722	Y723	Y724	Y725	Y726	Y727	Y728	Y729	Y730	Y731	Y732	Y733	Y734	Y735	Y736	Y737	Y738	Y739	Y740	Y741	Y742	Y743	Y744	Y745	Y746	Y747	Y748	Y749	Y750	Y751	Y752	Y753	Y754	Y755	Y756	Y757	Y758	Y759	Y760	Y761	Y762	Y763	Y764	Y765	Y766	Y767	Y768	Y769	Y770	Y771	Y772	Y773	Y774	Y775	Y776	Y777	Y778	Y779	Y780	Y781	Y782	Y783	Y784	Y785	Y786	Y787	Y788	Y789	Y790	Y791	Y792	Y793	Y794	Y795	Y796	Y797	Y798	Y799	Y800	Y801	Y802	Y803	Y804	Y805	Y806	Y807	Y808	Y809	Y810	Y811	Y812	Y813	Y814	Y815	Y816	Y817	Y818	Y819	Y820	Y821	Y822	Y823	Y824	Y825	Y826	Y827	Y828	Y829	Y830	Y831	Y832	Y833	Y834	Y835	Y836	Y837	Y838	Y839	Y840	Y841	Y842	Y843	Y844	Y845	Y846	Y847	Y848	Y849	Y850	Y851	Y852	Y853	Y854	Y855	Y856	Y857	Y858	Y859	Y860	Y861	Y862	Y863	Y864	Y865	Y866	Y867	Y868	Y869	Y870	Y871	Y872	Y873	Y874	Y875	Y876	Y877	Y878	Y879	Y880	Y881	Y882	Y883	Y884	Y885	Y886	Y887	Y888	Y889	Y890	Y891	Y892	Y893	Y894	Y895	Y896	Y897	Y898	Y899	Y900	Y901	Y902	Y903	Y904	Y905	Y906	Y907	Y908	Y909	Y910	Y911	Y912	Y913	Y914	Y915	Y916	Y917	Y918	Y919	Y920	Y921	Y922	Y923	Y924	Y925	Y926	Y927	Y928	Y929	Y930	Y931	Y932	Y933	Y934	Y935	Y936	Y937	Y938	Y939	Y940	Y941	Y942	Y943	Y944	Y945	Y946	Y947	Y948	Y949	Y950	Y951	Y952	Y953	Y954	Y955	Y956	Y957	Y958	Y959	Y960	Y961	Y962	Y963	Y964	Y965	Y966	Y967	Y968	Y969	Y970	Y971	Y972	Y973	Y974	Y975	Y976	Y977	Y978	Y979	Y980	Y981	Y982	Y983	Y984	Y985	Y986	Y987	Y988	Y989	Y990	Y991	Y992	Y993	Y994	Y995	Y996	Y997	Y998	Y999	Y1000	Y1001	Y1002	Y1003	Y1004	Y1005	Y1006	Y1007	Y1008	Y1009	Y1010	Y1011	Y1012	Y1013	Y1014	Y1015	Y1016	Y1017	Y1018	Y1019	Y1020	Y1021	Y1022	Y1023	Y1024	Y1025	Y1026	Y1027	Y1028	Y1029	Y1030	Y1031	Y1032	Y1033	Y1034	Y1035	Y1036	Y1037	Y1038	Y1039	Y1040	Y1041	Y1042	Y1043	Y1044	Y1045	Y1046	Y1047	Y1048	Y1049	Y1050	Y1051	Y1052	Y1053	Y1054	Y1055	Y1056	Y1057	Y1058	Y1059	Y1060	Y1061	Y1062	Y1063	Y1064	Y1065	Y1066	Y1067	Y1068	Y1069	Y1070	Y1071	Y1072	Y1073	Y1074	Y1075	Y1076	Y1077	Y1078	Y1079	Y1080	Y1081	Y1082	Y1083	Y1084	Y1085	Y1086	Y1087	Y1088	Y1089	Y1090	Y1091	Y1092	Y1093	Y1094	Y1095	Y1096	Y1097	Y1098	Y1099	Y1100	Y1101	Y1102	Y1103	Y1104	Y1105	Y1106	Y1107	Y1108	Y1109	Y1110	Y1111	Y1112	Y1113	Y1114	Y1115	Y1116	Y1117	Y1118	Y1119	Y1120	Y1121	Y1122	Y1123	Y1124	Y1125	Y1126	Y1127	Y1128	Y1129	Y1130	Y1131	Y1132	Y1133	Y1134	Y1135	Y1136	Y1137	Y1138	Y1139	Y1140	Y1141	Y1142	Y1143	Y1144	Y1145	Y1146	Y1147	Y1148	Y1149	Y1150	Y1151	Y1152	Y1153	Y1154	Y1155	Y1156	Y1157	Y1158	Y1159	Y1160	Y1161	Y1162	Y1163	Y1164	Y1165	Y1166	Y1167	Y1168	Y1169	Y1170	Y1171	Y1172	Y1173	Y1174	Y1175	Y1176	Y1177	Y1178	Y1179	Y1180	Y1181	Y1182	Y1183	Y1184	Y1185	Y1186	Y1187	Y1188	Y1189	Y1190	Y1191	Y1192	Y1193	Y1194	Y1195	Y1196	Y1197	Y1198	Y1199	Y1200	Y1201	Y1202	Y1203	Y1204	Y1205	Y1206	Y1207	Y1208	Y1209	Y1210	Y1211	Y1212	Y1213	Y1214	Y1215	Y1216	Y1217	Y1218	Y1219	Y1220	Y1221	Y1222	Y1223	Y1224	Y1225	Y1226	Y1227	Y1228	Y1229	Y1230	Y1231	Y1232	Y1233	Y1234	Y1235	Y1236	Y1237	Y1238	Y1239	Y1240	Y1241	Y1242	Y1243	Y1244	Y1245	Y1246	Y1247	Y1248	Y1249	Y1250	Y1251	Y1252	Y1253	Y1254	Y1255	Y1256	Y1257	Y1258	Y1259	Y1260	Y1261	Y1262	Y1263	Y1264	Y1265	Y1266	Y1267	Y1268	Y1269	Y1270	Y1271	Y1272	Y1273	Y1274	Y1275	Y1276	Y1277	Y1278	Y1279	Y1280	Y1281	Y1282	Y1283	Y1284	Y1285	Y1286	Y1287	Y1288	Y1289	Y1290	Y1291	Y1292	Y1293	Y1294	Y1295	Y1296	Y1297	Y1298	Y1299	Y1300	Y1301	Y1302	Y1303	Y1304	Y1305	Y1306	Y1307	Y1308	Y1309	Y1310	Y1311	Y1312	Y1313	Y1314	Y1315	Y1316	Y1317	Y1318	Y1319	Y1320	Y1321	Y1322	Y1323	Y1324	Y1325	Y1326	Y1327	Y1328	Y1329	Y1330	Y1331	Y1332	Y1333	Y1334	Y1335	Y1336	Y1337	Y1338	Y1339	Y1340	Y1341	Y1342	Y1343	Y1344	Y1345	Y1346	Y1347	Y1348	Y1349	Y1350	Y1351	Y1352	Y1353	Y1354	Y1355	Y1356	Y1357	Y1358	Y1359	Y1360	Y1361	Y1362	Y1363	Y1364	Y1365	Y1366	Y1367	Y1368	Y1369	Y1370	Y1371	Y1372	Y1373	Y1374	Y1375	Y1376	Y1377	Y1378	Y1379	Y1380	Y1381	Y1382	Y1383	Y1384	Y1385	Y1386	Y1387	Y1388	Y1389	Y1390	Y1391	Y1392	Y1393	Y1394	Y1395	Y1396	Y1397	Y1398	Y1399	Y1400	Y1401	Y1402	Y1403	Y1404	Y1405	Y1406	Y1407	Y1408	Y1409	Y1410	Y1411	Y1412	Y1413	Y1414	Y1415	Y1416	Y1417	Y1418	Y1419	Y1420	Y1421	Y1422	Y1423	Y1424	Y1425	Y1426	Y1427	Y1428	Y1429	Y1430	Y1431	Y1432	Y1433	Y1434	Y1435	Y1436	Y1437	Y1438	Y1439	Y1440	Y1441	Y1442	Y1443	Y1444	Y1445	Y1446	Y1447	Y1448	Y1449	Y1450	Y1451	Y1452	Y1453	Y1454	Y1455	Y1456	Y1457	Y1458	Y1459	Y1460	Y1461	Y1462	Y1463	Y1464	Y1465	Y1466	Y1467	Y1468	Y1469	Y1470	Y1471	Y1472	Y1473	Y1474	Y1475	Y1476	Y1477	Y1478	Y1479	Y1480	Y1481	Y1482	Y1483	Y1484	Y1485	Y1486	Y1487	Y1488	Y1489	Y1490	Y1491	Y1492	Y1493	Y1494	Y1495	Y1496	Y1497	Y1498	Y1499	Y1500	Y1501	Y1502	Y1503	Y1504	Y1505	Y1506	Y1507	Y1508	Y1509	Y1510	Y1511	Y1512	Y1513	Y1514	Y1515	Y1516	Y1517	Y1518	Y1519	Y1520	Y1521	Y1522	Y1523	Y1524	Y1525	Y1526	Y1527	Y1528	Y1529	Y1530	Y1531	Y1532	Y1533	Y1534	Y1535	Y1536	Y1537	Y1538	Y1539	Y1540	Y1541	Y1542	Y1543	Y1544	Y1545	Y1546	Y1547	Y1548	Y1549	Y1550	Y1551	Y1552	Y1553	Y1554	Y1555	Y1556	Y1557	Y1558	Y1559	Y1560	Y1561	Y1562	Y1563	Y1564	Y1565	Y1566	Y1567	Y1568	Y1569	Y1570	Y1571	Y1572	Y1573	Y1574	Y1575	Y1576	Y1577	Y1578	Y1579	Y1580	Y1581	Y1582	Y1583	Y1584	Y1585	Y1586	Y1587	Y1588	Y1589	Y1590	Y1591	Y1592	Y1593	Y1594	Y1595	Y1596	Y1597	Y1598	Y1599	Y1600	Y1601	Y1602	Y1603	Y1604	Y1605	Y1606	Y1607	Y1608	Y1609	Y1610	Y1611	Y1612	Y1613	Y1614	Y1615	Y1616	Y1617	Y1618	Y1619	Y1620	Y1621	Y1622	Y1623	Y1624	Y1625	Y1626	Y1627	Y1628	Y1629	Y1630	Y1631	Y1632	Y1633	Y1634	Y1635	Y1636	Y1637	Y1638	Y1639

