BV-BRC SARS-CoV-2 Emerging Variant Report
January 17, 2023

Details of the emerging variants analysis can be found in "BV-BRC SARS-CoV-2 Emerging Variant Report – 20230117.xlsx" based on sequence data from GISAID.

Keep in mind that the information provided reflects sequence counts and sequence proportions and, as such, is impacted by sampling bias in the sequence databases and should not be interpreted as the prevalence of disease caused by these variants.

In addition, due to sequence anomalies (e.g., ambiguous nucleotides in many sequence records) and other issues, the absolute counts of Variants of Concern sequences are likely to be underestimates of the true sequence prevalence.

This report includes preliminary/incomplete stats for the month of January in order to identify early signs of novel variants emerging.

The key findings are summarized below.

USA – VOC

OMICRON

- Based on CDC Nowcast estimates (https://covid.cdc.gov/covid-data-tracker/#variant-proportions) for the week ending 1/14/2023 in the US in order of prevalence (note that the Nowcast estimates are senstitive to sampling bias and updates to the PANGO annotations):
  - ***XBB.1.5 has rapidly emerged and become one of the predominant variants over the last month and is currently estimated at 43.0% in the U.S., a significant rise from 20.1 in December***
  - **BQ.1.1** is currently estimated at 28.8%, down from 36.3% in December
  - **BQ.1** is currently estimated at 15.9%, down from 22.9% in December
  - The original **XBB** is currently estimated at 3.9%, down from 5.0% in December
  - **BA.5** is currently estimated at 3.7%, down from 6.0% in December
  - **BN.1** is currently estimated at 2.1%, down from 3.1% in December
  - **BF.7** is currently estimated at 1.4%, down from 2.9% in December
  - **BA.2.75** is currently estimated at 1.3%, essentially flat from 1.4% in December
  - **BA.5.2.6** is currently estimated at 0.5%, down from 0.9% in December
  - **BA.4.6** is currently estimated at 0.1%, down from 0.4% in December
- ***XBB.1.5***
  - ***Appears to have emerged in the northeastern U.S. (NY & CT) in October 2022***
  - ***Recombinant between two different BA.2 subvariants - BJ.1 and BA.2.75***
  - ***Has an F486P substitution in S instead of the F486S found in the S of XBB***
  - ***Likely founder differs from ancestral Wuhan 1 by the following substitutions in S:***
    - ***T19I,L24-,P25-,P26-,A27S,V83A,G142D,Y144-,H146Q,Q183E,V213E,G339H,R346T,L368I,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,V445P,G446S,N460K,S477N,T478K,E484A,F486P,F490S,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K***

    - ***The XBB.1.5 sub-lineage predominant in December has also acquired the G252V substitution***
    - ***Note that the Y144-, H146Q annotation from GISAID is equivalent to Y145Q, H146- at the amino acid level; the latter is probably the correct translation from the nucleotide sequence***
    - ***The F486P substitution likely increases affinity for ACE2 receptor***
    - ***Neutralization of XBB and XBB.1 (and likely XBB.1.5) by sera from vaccinees and infected persons was markedly impaired - https://www.biorxiv.org/content/10.1101/2022.11.23.517532v1.full.pdf***
    - ***Monoclonal antibodies capable of neutralizing the original Omicron variant, including those with Emergency Use Authorization, were largely inactive against the XBB and XBB.1 subvariants (and likely XBB.1.5) - https://www.biorxiv.org/content/10.1101/2022.11.23.517532v1.full.pdf***
- ***XBB***
    - ***Likely founder differs from ancestral Wuhan 1 by the following substitutions in S: T19I,L24-,P25-,P26-,A27S,V83A,G142D, Y144-,H146Q,Q183E,V213E,G339H,R346T,L368I,S371F,S373P,S375F,T376A,D405N, R408S,K417N,N440K,V445P,G446S,N460K,S477N,T478K,E484A,F486S,F490S, Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K***
    - ***The XBB sub-lineage predominant in December has acquired the additional G252V substitution***
    - ***Note that the Y144-, H146Q annotation from GISAID is equivalent to Y145Q, H146- at the amino acid level; the latter is probably the correct translation from the nucleotide sequence***
- Based on BV-BRC analysis of comprehensive data from GISAID, listed below are lineages with sequence prevalence >1.0% or a growth rate >3 fold and count >10 in January so far (ranked in order of sequence prevalence; total number of sequence for January – 1000, is still quite small). Lineages with fold growth >3 from December to January so far are highlighted in ***bold italic***:
    - **BQ.1.1** - 18%, 1.0 fold growth
    - **XBB.1.5** - 17%, 2.5 fold growth
    - **BQ.1** – 5.6%, 0.65 fold growth
    - **XBB.1** – 3.4%, 1.1 fold growth
    - **BQ.1.1.5** – 3.3%, 1.6 fold growth
    - **BQ.1.1.22** – 3.0%, 1.2 fold growth
    - **BQ.1.2** - 2.7%, 1.4 fold growth
    - **BQ.1.1.18** – 2.3%, 1.6 fold growth
    - **BQ.1.3** – 2.1%, 1.1 fold growth
    - **BQ.1.1.4** – 1.9%, 0.80 fold growth
    - **CH.1.1** – 1.6%, 2.9 fold growth
    - **BQ.1.13** – 1.5%, 1.4 fold growth
    - **BF.7** – 1.5%, 0.75 fold growth
    - **BA.5.1** – 1.4%, 1.5 fold growth
    - **BA.5.2** – 1.4%, 0.84 fold growth
    - ***BQ.1.1.7 – 1.3%, 3.1 fold growth***

DELTA (**B.1.617.2** and **AY** sub-lineages) *(no significant change since previous report)*

- One Delta sequence in the US in December; six in November; none in January so far

USA – (other VOCs and VOIs) *(no significant change since previous report)*

- None

USA – Recombinants

- **XBB.1.5** - 172 sequences (out of 1000) in January so far; 4303 sequences (out of 62411) in December
- **XBB.1** - 34 sequences in January so far; 1861 sequences in December
- **XBB.2** - 8 sequences in January so far; 401 sequences in December
- **XBB** - 7 sequences in January so far; 172 sequences in December
- **XBF** - 2 sequences in January so far; 64 sequences in December
- **XBB.3** - 1 sequence in January so far; 77 sequence in December
- **XBB.4** - no sequences in January so far; 29 sequences in December
- **XBB.1.1** - no sequences in January so far; 28 sequences in December
- **XBB.1.4** - no sequences in January so far; 10 sequences in December
- **XBC.1** - no sequences in January so far; 10 sequences in December
- **XBD** - no sequences in January so far; 10 sequences in December
- **XBB.1.3** - no sequences in January so far; 4 sequences in December
- **XBJ** - no sequences in January so far; 4 sequences in December
- **XBG** - no sequences in January so far; 3 sequences in December
- **XBE** - no sequences in January so far; 3 sequences in December
- **XBB.1.4.1** - no sequences in January so far; 2 sequences in December
- **XBB.3.1** - no sequences in January so far; 2 sequences in December
- **XBH** - no sequences in January so far; 2 sequences in December
- **XAY.1** - no sequences in January so far; 1 sequence in December

World – VOC

OMICRON

- Omicron remains dominant globally. Listed below are lineages showing the highest sequence prevalence (> 2.0%) or a fold growth > 3 fold and count >50 in January so far. Lineages with fold growth >3 from December to January are highlighted in ***bold italic***:
  - **BQ.1.1** - 13%, 0.88 fold growth
  - **CH.1.1** – 8.3%, 3.6 fold growth
  - **BQ.1.1.22** – 5.5%, 1.8 fold growth
  - **XBB.1.5** – 5.0%, 2.1 fold growth
  - **BQ.1.1.20** – 4.7%, 4.2 fold growth
  - **CH.1.1.1** – 2.6%, 3.6 fold growth
  - **XBB.1** – 2.5%, 0.86 fold growth
  - **BN.1.3.1** – 2.3%, 2.8 fold growth
  - **BF.7** – 2.3%, 0.62 fold growth
  - **BQ.1** – 2.1%, 0.48 fold growth
  - ***BA.5.11 – 1.6%, 3.5 fold growth***
  - ***CH.1.1.2 - 0.8%, 4.7 fold growth***

- ***CJ.1 - 0.58%, 3.4 fold growth***
- ***BN.1.2.1 - 0.56%, 3.9 fold growth***
- ***XAY.2 - 0.53%, 4.0 fold growth***

- Substitutions in spike that we are monitoring (>3 fold growth from December to January with counts >50) include those listed below (but note that the numbers are still relatively small for some of these). Substitutions with sequence prevalence >1.0% in January so far are highlighted in ***bold italic***::
  - **L24S** - 0.69%, 10 fold growth
  - **V70I** - 0.73%, 6.8 fold growth
  - **E1144Q** - 0.67%, 5.6 fold growth
  - **T470N** - 0.57%, 3.9 fold growth
  - **R21G** - 0.53%, 3.4 fold growth
  - ***N185D – 2.7%, 3. 4 fold growth***
  - **T19R** - 0.53%, 3.3 fold growth
  - **L18F** - 0.54%, 3.2 fold growth
  - **A1070V** - 0.72%, 3.2 fold growth
  - **N148-** - 0.94%, 3.2 fold growth
  - **K147-** - 0.94%, 3.1 fold growth
  - **E156G** - 0.78%, 3.1 fold growth
  - **R158-** - 0.78%, 3.0 fold growth

Convergent mutations in the N-Terminal Domain (NTD) of the Spike protein: (more information here)

- We noticed a sharp increase in mutations located in the NTD in the past three months (November 2022 – January 2023)
- The majority of these mutations occur in structural loops know as N1-N5 loops, especially the N3 loop
- Evidence exists that these NTD mutations are highly convergent
- Evidence suggest that these mutations result in antigenic escape
- These NTD mutations also occur in other VOCs and long-term infections
- NTD mutations may occur sequentially after RBD escape mutations occur
- ***Details about these NTD substitutions can be found in previous reports***

DELTA (**B.1.617.2**, **AY** sub-lineages and some **X** recombinants)

- 255 Delta genomes in December (mostly XAY.2 in Denmark); 52 in January so far

World (other VOIs)

- none in December

World – Recombinants (ranked in order of prevalence)

- **XBB.1.5** - 496 sequences (out of 9834) in January so far; 5305 sequences (out of 220217) in December
- **XBB.1** - 244 sequences in January so far; 6351 sequences in December
- **XBF** - 145 sequences in January so far; 1516 sequences in December
- **XAY.2** - 52 sequences in January so far; 288 sequences in December
- **XBB.2** - 48 sequences in January so far; 2143 sequences in December
- **XBB.1.4.1** - 35 sequences in January so far; 483 sequences in December

- **XBC.1** - 26 sequences in January so far; 272 sequences in December
- **XBB** - 15 sequences in January so far; 503 sequences in December
- **XBB.1.1** - 8 sequences in January so far; 218 sequences in December
- **XBB.3** - 6 sequences in January so far; 174 sequences in December
- **XBB.1.4** - 4 sequences in January so far; 116 sequences in December
- **XBJ** - 3 sequences in January so far; 39 sequences in December
- **XBB.3.1** - 3 sequences in January so far; 23 sequences in December
- **XBG** - 2 sequences in January so far; 23 sequences in December
- **XAZ** - 1 sequence in January so far; 13 sequences in December
- **XBB.4** - no sequences in January so far; 103 sequences in December
- **XBD** - no sequences in January so far; 32 sequences in December
- **XAY.1** - no sequences in January so far; 30 sequences in December
- **XAY.1.1** - no sequences in January so far; 12 sequences in December
- **XBB.1.3** - no sequences in January so far; 8 sequences in December
- **XBE** - no sequences in January so far; 7 sequences in December
- **XAY** - no sequences in January so far; 6 sequences in December
- **XBH** - no sequences in January so far; 4 sequences in December
- **XBC.2** - no sequences in January so far; 3 sequences in December
- **XBB.5** - no sequences in January so far; 2 sequences in December
- **XAS** - no sequences in January so far; 1 sequence in December

China

- Data from China is somewhat limited; only 752 sequences reported in December (only 21 in January so far)
- The proportion of the currently circulating lineages in China (count > 5) are quite different from the rest of the world:
    - **BF.7** - 36%, 1.4 fold growth
    - **BA.5.2** - 35%, 1.2 fold growth
    - **BQ.1.1** – 4.4%, 0.51 fold growth
    - **BA.5.2.1** – 2.1%, 0.66 fold growth
    - **XBB.1** – 1.7%, 0.53 fold growth
    - **BQ.1** – 1.5%, 0.54 fold growth
    - **BA.2** – 1.3%, 1 fold growth
    - **BA.5.1** – 1.2%, 1.1 fold growth
    - **BN.1.3** – 1.1%, 0.65 fold growth

Variants that have been mentioned in the media and/or social media:

- Differences Between Reported COVID-19 Deaths and Estimated Excess Deaths in Counties Across the United States, March 2020 to February 2022
- Extraordinary Evasion of Neutralizing Antibody Response by Omicron XBB.1.5, CH.1.1 and CA.3.1 Variants
- COVID-19 Induces Senescence and Exhaustion of T Cells in Patients with Mild/Moderate and Severe Disease during a Seven-Day Interval

- Enhanced transmissibility, infectivity and immune resistance of the SARS-CoV-2 Omicron XBB.1.5 variant
- A Systematic Review and Meta-analysis of the Association Between SARS-CoV-2 Vaccination and Myocarditis or Pericarditis
- Effect of the third dose of BNT162b2 COVID-19 mRNA vaccine on anti-SARS-CoV-2 antibody levels in healthcare workers
- Pulmonary function three to five months after hospital discharge for COVID-19: a single centre cohort study
- Reinfection rate in a cohort of healthcare workers over 2 years of the COVID-19 pandemic
- Long COVID: major findings, mechanisms and recommendations