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Closing the Barn Door Before All the Horses Escape: The Need for Continued Monitoring of COVID-19 Variants

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Description

January 2023 marks three years since the first genetic sequence of SARS-CoV-2 (Wuhan-Hu-1) was made publicly available [1]. As of 2023, >14 million sequences of SARS-CoV-2 were published in the database for the Global Initiative on Sharing Avian Flu Data (GISAID), EpiCoV Database [2]. SARS-CoV-2 variants emerge as thousands of unique sequences, evolving independent of homologous viral populations. Risks of emerging variants to public health include:

i) Transmissibility

ii) Disease severity

iii) Immune escape

iv) Diagnostics performance

v) Therapeutic escape/efficacy

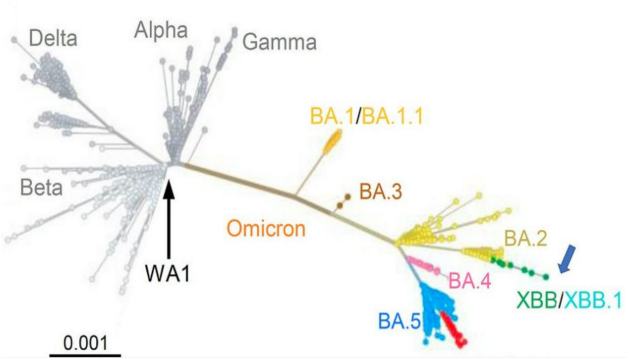
Variant tracking is limited, in part because United States (US) laboratory billing does not cover variant testing as a diagnostic or surveillance test. Sequencing is expensive, difficult to scale/mobilize and subject to long sample-to-result times. Surveillance efforts fail to test enough cases, leading to delayed detection of novel variants at best and at worst, leaves new variants undetected until they have infected a majority of a population.

We urge engaged parties (industry, government, clinical laboratories, and academics, public health leaders) to consider the use of variant tracking on a national level, within the repertoire of CLIA certified laboratories, as a targeted, scalable, cost-effective approach within public health policies.

In the US, genomic surveillance operates through the CDC National SARS-CoV-2 Strain Surveillance (NS3). However, requests for specimens' total only 750-1000 specimens/week [3] equating to a reporting rate of <25 cases/month/100,000 persons [4]. Outside the US, low- and middle-income countries test 27 cases/100,000 persons per day [4]. On Sample size estimationssuggest that low testing testing rates result in smaller virus specimen pools, intermittent sampling biases, and sporadic reporting [5-8]. Predictive modeling, suggests detection of viral variants occurs 1-3 weeks earlier if testing rates increase to ~100 tests/100,000 people/day [9]. A strategy which can be accomplished by increasing testing within US clinical laboratories [8].

Lai et al. introduced single nucleotide polymorphism RT-PCR testing within routine "marker panels" as an opportunity for predictive, rapid, accessible variant detection employed within US-s [10]. This approach overcomes expense, low throughput, long turn-around-times and lack of visibility for submitting laboratories.

Recent sub-variants, XBB, highlight the need to track variants earlier through coordinated global testing strategies. XBB is a recombinant (fusion) of BA.2 and BA.2.75 Omicron variants (Figure 1) [11].



The XBB1.5 variant carries F486P mutation in the receptor binding domain region of SARS-2 CoV-2, a mutation affecting ACE2 receptor binding strength.

While, studies suggest XBB1.5 is not more immune evasive than previous variants, it displays tighter binding affinity to ACE2 receptors, resulting in its high transmissibility [12].

The CDC has recently expanded voluntary surveillance testing

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among international travelers [13] and government funding for wastewater testing is expanding [13]. Despite these initiatives, testing needs to reach environments where cases present. Coordination between clinical laboratories and government is required. In communities first affected, academic and clinical laboratories were not utilized in the critical early weeks when the virus spread undetected. Three years later, tracking of viral variants is unquestionably part of public health strategy. Access to easy-to use, widespread testing remains key in efforts to "close the door" before variants emerge.

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