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Leveraging a Public-Private-Academic Collaborative Partnership to Confront Challenges in the COVID-19 Pandemic

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ABSTRACT

Like all viruses, the SARS-CoV-2 virus mutates over time, creating new viral variants that have the potential to transmit more rapidly, cause more severe disease, or avoid treatment and prevention strategies. A critical component of the public health response to COVID-19 is identifying and tracking the emergenc of SARS-CoV-2 variants. In West Virginia, this effort is coordinated via a public-private-academic collaboration.

KEYWORDS

SARS-CoV-2, COVID-19, Epidemiology, Genomics, Sequencing

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Following the initial outbreak of COVID-19 in December 2019 and its spread to the United States in the following two months, initial efforts were focused on quickly and accurately diagnosing the disease. The predominant form of test developed uses reverse real-time reverse-transcriptase polymerase chain reaction (rRT-PCR) on samples, typically obtained via a nasopharyngeal swab. rRT-PCR is a common and relatively simple laboratory procedure and in the United States a number of commercial laboratories who were already equipped to perform this test quickly mobilized to provide large-capacity testing nationwide.

As with all viruses, the RNA replication of SARS-CoV-2, the virus causing COVID-19, is imperfect. Because of this, new genetic variants of the virus emerge over time. Some of these genetic variants, particularly those involving specific mutations in the S gene, which translates to the spike protein, confer evolutionary advantages[1]. These advantages may include increased transmissibility and/or the potential for more severe disease and as such pose an increased public health risk. There is the potential for genetic variation in the virus to cause decreased susceptibility to treatment or vaccination. At the time of writing, the Centers for Disease Control (CDC) has classified five specific variants as "variants of concern". Using the PANGOLIN nomenclature, these variants of concern are B.1.1.72, first discovered in the United Kingdom in October 2020, B.1.3513, first seen in South Africa in December 2020, P.14, first observed in Japan in January 2021 in patients who had recently traveled from Brazil and later observed in samples from Brazil which were collected in December 2020, and B.1.427 and B.1.4295, which were both first observed in California in July 2020. The CDC has identified three further variants which are classified as "variants of interest". The "variants of high consequence" category, which is intended for the variants most threatening to public health, currently has no variants assigned to it.

Identifying and tracking the prevalence of genetic variants of SARS-CoV-2 has become a public health priority. By identifying SARS-CoV-2 variants, epidemiologists can identify which variants have increased transmissibility as well as detect occurrences of known variants of concern. This in turn allows them to rapidly perform contact tracing and, if necessary, implement public health policies to mitigate the spread of more transmissible forms of the virus. Determining the variant of a particular viral sample

requires sequencing all 29,903 nucleotides in the viral genome. By contrast to diagnostics by rRT-PCR, this requires highly specialized, high-throughput sequencing technology and technical expertise both in laboratory processes and in data analysis.

In December 2020, the West Virginia "Coronavirus Czar" and Dean of the School of Medicine at West Virginia University, Dr. Clay Marsh, asked Dr. Laura Gibson, senior vice president for research at the WVU Health Sciences Center, to assemble a team to perform viral sequencing from positive SARS-CoV-2 samples from across the state. Dr. Gibson leveraged the genomics core facilities at WVU and Marshall University, the bioinformatics core facility at Marshall University, the state epidemiology laboratory at the WV Department of Health and Human Resources (DHHR), and WVU and commercial testing facilities across the state in order to develop a pipeline to identify SARS-CoV-2 variants. The WVU and Marshall University components of this team have a record of close collaboration spanning over a decade. The development of this pipeline requires complex logistics in moving samples from testing labs to sequencing labs and maintaining records of the origin of each sample while protecting private health information. Sequencing laboratory protocols had to be tested and optimized. A data analysis pipeline had to be developed, and high-performance computing resources were required in order to run it. Information management protocols for dissemination of occurrences of variants of concern to the DHHR and the state governor's coronavirus task force had to be implemented. The first sequencing run was completed on February 19th 2021 at the WVU genomics core facility and resulted in the detection of three samples with the B.1.1.7 variant. At the time of writing, eight sequencing runs have been completed, identifying the variant of 1,686 individual samples. These samples are drawn both from "surveillance" of predominantly asymptomatic subjects and clinical samples from symptomatic patients. The resulting data set can be used, for example, to visualize the change of distribution of the different variants across time (Figure 1).

All five variants of concern have been detected in the state. The last to be detected was P.[1] on April 16th 2021; contact tracing was initiated and the public

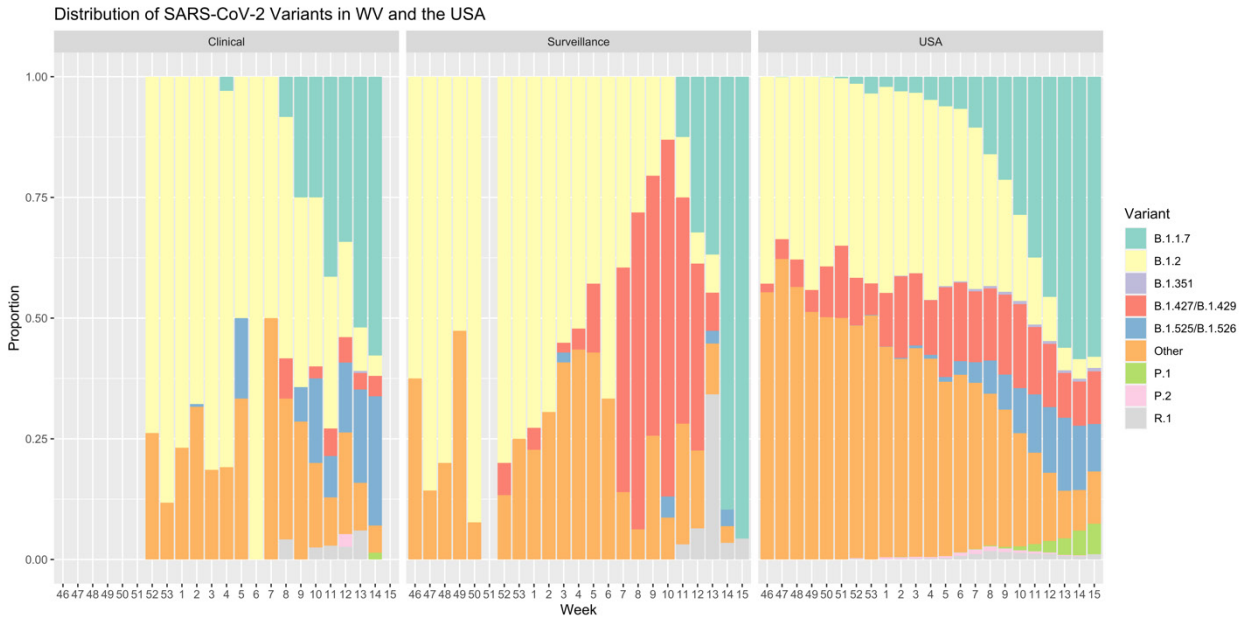

FIGURE 1. Change in distribution of selected SARS-CoV-2 variants in West Virginia among sequenced clinical (left panel) and surveillance (middle panel) samples, showing the emergence and eventual dominance of B.1.1.7 over the B.1.2 variant. For comparison, the distribution across the USA over the same time period is shown (right panel), using data downloaded from NCBI GenBank.

was informed within hours of the completion of sequencing in the laboratory. Sequences from these samples, along with metadata, have been submitted to the Global Initiative on Sharing All Influenza Data (GISAID) in order to contribute to global epidemiology and other data analyses.

The rapid development of this pipeline was only possible by leveraging specific technical expertise, dedicated specialized equipment, and existing collaborations that are almost uniquely present in academic environments. The academic core facilities that provide this functionality are supported in part by investments in the form of grant funding from the National Institute for General Medical Sciences. The academic entities collaborate with corporate laboratories that provide the positive samples and the DHHR who enact the public health policies in response to the scientific findings.

This one-of-a-kind, public-private-academic partnership demonstrates the value of public investment in academic institutions and how the ongoing support of science can contribute to the well-being of society, particularly in times of a public health emergency.

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