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How COVID-19 Variants Get Their Name

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Viruses have figured central in American life over the last 18 months, with the emergence of a new member of the Coronavirus family adapted to humans. At the end of 2019, a new coronavirus began to infect Chinese citizens; symptoms included fever and pneumonia-like congestion with an alarming number of patients dying from respiratory failure. Efforts to contain the spread became increasingly stringent, including a strict curfew, calls to physically distance from non-family members, face mask mandates, and an increased focus on hand washing and cleaning and disinfecting surfaces. While these measures had some impact, they did not prevent the virus from spreading rapidly to other countries, and in March 2020, the World Health Organization (WHO) declared a global pandemic.

Early in the outbreak, samples were sequenced, and the causal agent named SARS-CoV-2 (sudden acute respiratory syndrome coronavirus). The first fully sequenced genome was labeled Wuhan-1 and became the 'template' to which all following sequences have been compared. After a few months of sequencing samples, enough data was collected to calculate the mutation rate as 1 new mutation per 10 people infected. An article published in July 2020 by the WHO shows the significance of the mutation rate. The article reports, from the 10,022 genomes sequences taken from patients residing in 68 countries, 5775 distinct variants were observed, segregating into 6 distinct major clades and 14 subclades (clades denote relationships shared by genetic similarity, like inheritance). If we place the start of the infection in November 2019, then within 8 months, over 5000 distinct variants can be identified. Variant identification requires an understanding of genetic mutations and classifying lineages based on these differences. This article will not delve deep into those biology principles but will provide highlights significant to understanding variant identification.

All viruses share a general life cycle: they bind to cell surfaces and enter the cell, replicate their genome, package up the new replicates, and emerge from the cell to infect new cells. If errors occur in the replication of the genome, mutations develop; these are termed strains or variants. The entire SARS-CoV-2 genome is approximately 30,000 bp in length. Several methods are available to accomplish sequencing of the genome, the most popular being the

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Practice Guidelines

The following practice guidelines have been developed by the Clinical Laboratory Advisory Council. They can be accessed at the LQA website.

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How COVID-19 Variants Get Their Name

ARTIC version 3 method. This method divides the genome into segments using PCR (polymerase chain reaction) such that each segment overlaps the previous and following segments. The segments are sequenced, and the reads are assembled like overlapping puzzle pieces so that the genome is reconstructed. The assembled genome can then be compared to the Wuhan-1 genome and all the nucleotide changes noted as well as insertions and deletions.

In the first few months of the pandemic a new bioinformatics program called Pangolin was developed. Pangolin relies on a novel algorithm called pangoLEARN. This new approach classifies the newly sequenced genome against all the diverse lineages present instead of a representative select sequences. It compares the new genome against the large, diverse population of sequenced strains using a newly developed IT approach termed machine learning. As the large dataset grows, the program learns and can quickly segregate the new genome into the proper clade based on the complete sequence.

Lineage names are related to this classification, but are not independent from human oversight. Two committees, comprised of very qualified subject matter experts, determine whether a new lineage name is warranted based on the data (mutations and clade assignments). These lineage determinations are incorporated into algorithms for rapid, computerized method for identification of newly sequenced strains. Each lineage identification is based on the mutation types identified in the compiled sequence, and somewhat on clade assignment resulting in names like B.1.14 and B.1.627.2. In these examples, B is one of two lineages that emerged early in the pandemic. The first lineage in that group is B.1. As significant branching in the lineage occurs, new assignments are made. It doesn't take too long for the lineage names to get clumsy, sometimes resulting in an alias name. For example: remember B.1.1.28.1? It got an alias name: P.1.

If you were to map all the mutations across the length of the genome, you would see that the entire length is marked fairly evenly with changes. This means that no one region is mutating faster than another. But one specific protein, the spike protein, is of particular interest to both virologists and public health officials. This focus comes from two points: 1) the protein drives binding to the cell surface and entry into the cell; and 2) several mutations in this protein appear to enhance this function because these variants are associated with higher rates of infection (greater virulence). These variants have earned the name "Variants of Concern." The WHO recommends using letters of the Greek alphabet to denote variants of concern . The most common one in Washington State now is Delta, which corresponds to B.1.617.2 and its associated sublineages of AY.1, AY.2, and AY.3. Prediction models suggest that the large array of variants present throughout the pandemic will soon become a smaller number of circulating strains. Virologists and public health officials are watching carefully to determine if emerging cases are the result of reduced vaccine efficacy, and if this reduced efficiency is the result of additional mutations. Physical methods have worked (masks, distance, increased sanitation methods), but vaccines are still the best method for controlling this new disease and keeping people out of the hospital. Washington State Department of Health tracks variants by conducting sequencing on a subset of positive SARS-CoV-2 cases from across the state. Several laboratories contribute to these critical efforts by submitting specimens to the public health laboratory for sequencing, and some are sequencing on their own. The results of these sequencing efforts are published weekly on the DOH website. The contribution of clinical labs to public health has been tremendous, and the time and effort put into forwarding requested specimens is greatly appreciated.

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Table 1. Currently tracked variants of concern

Varient of Concern	**WHO Label**	**FIrst Detected in World**	**First Detected in Washington State**
B.1.1.7	Alpha	United Kingdom, September 2020	January 2021
B.1.351, B.1.351.1, B.1.351.2, B.1.351.3	Beta	South Africa, December 2020	February 2021
P.1, P.1.1, P.1.2	Gamma	Brazil, April 2020	March 2021
B.1.617.2, AY.1, AY.2, AY.3	Delta	India, October 2020	April 2021

RESERVE THE DATE

CLINICAL LABORATORY CONFERENCE

NOVEMBER 8, 2021

More details to follow in upcoming issues of Elaborations

Calendar of Events

Training Classes:

2021 Joint Spring Seminar
Sponsored by ASCLS-WA, ASCLS-OR, ASCLS-AK
April 21-23 Virtual Event

2021 Northwest Medical Laboratory Symposium
October 6-9 Virtual Event

2021 Clinical Laboratory Conference

November 8 Tukwila

Contact information for the events listed above can be found on page 2. The Calendar of Events is a list of upcoming conferences, deadlines, and other dates of interest to the clinical laboratory community. If you have events that you would like to have included, please mail them to ELABORATIONS at the address on page 2. Information must be received at least one month before the scheduled event. The editor reserves the right to make final decisions on inclusion

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