COVID-19 could outwit science unless knowledge stays current

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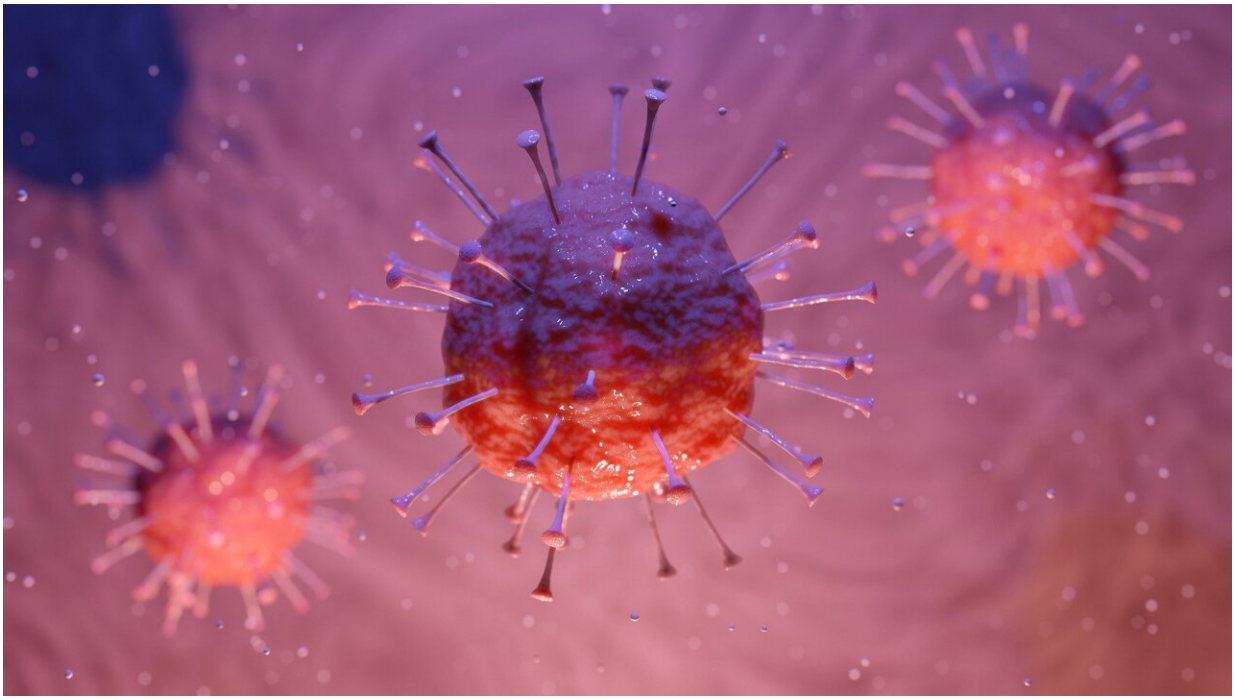

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The virus that causes COVID-19 has many variants, and if scientists don't stay on top of how it is changing in different parts of the world, testing for it may produce false negative results.

The development of an effective vaccine could also be hampered if experts don't constantly sequence samples of the virus to track its genetic

diversity.

These insights arise from a study by researchers in the University of Manitoba's Rady Faculty of Health Sciences in collaboration with a virology lab at Universidad de Concepción in Chile. The study was published online in May in *PeerJ*—the Journal of Life and Environmental Sciences.

The researchers used publicly available datasets to analyze whole genome sequencing samples from patients who were infected with SARS-CoV-2, the virus that causes COVID-19, before March 27, 2020.

Dr. Carlos Farkas, a postdoctoral researcher in pharmacology and therapeutics in the Max Rady College of Medicine and at the Research Institute in Oncology and Hematology, is the study's lead author. He is at the forefront of using novel tools in bioinformatics (the science of using computers to analyze biological data) to track mutations of the coronavirus.

The UM team was the first to combine genomic sequencing data from two worldwide sources in order to detect variants by geographic region. They found 146 different variants, or genetic "footprints" left by the virus, in the patient data.

"One of our key findings was that samples from Washington, one of the U.S. states where the virus was first detected, had quite a distinctive footprint of specific viral sequence changes," said co-author Dr. Jody Haigh, associate professor of pharmacology and therapeutics and senior scientist at the Research Institute in Oncology and Hematology.

"About 39 percent of Washington State samples had this footprint. Asian and European samples were more diverse in terms of changes in viral sequence, but their footprints were clearly different from those in the

U.S. samples."

The lab test that is used to detect SARS-CoV-2, Farkas and Haigh said, uses small pieces of DNA, or primers, that bind to the viral sequence and amplify any viral RNA/DNA that is present in the patient sample.

"These primers need to match the viral sequence exactly in order to produce a robust positive result," Farkas said. "If researchers design these primers to bind to regions of the virus that they don't realize have changed in a particular population, there may be poor amplification and the result can be false negatives."

The UM researchers found that some changes in viral sequence were indeed located in regions of the virus where primers were supposed to bind. "This may explain some of the false negative results in COVID-19 testing," Haigh said.

"Because SARS-CoV-2 is changing rapidly, researchers should be aware of its current local viral footprints in order to design DNA primers that don't bind to regions of the virus that have changed. Other regions of the virus that don't show these changes should be used for designing primers."

The researchers hope their results will influence COVID-19 testing and vaccine development and highlight the importance of frequent genetic sequencing of samples in every country of the world.

The study team, in collaboration with BioXplor, a data-driven drug discovery platform, has recently obtained funding from Mitacs to develop new online software tools. These tools will allow researchers to continuously track changes in viral sequence and to design primers that avoid viral change "hotspots."

More information: Carlos Farkas et al. Insights on early mutational events in SARS-CoV-2 virus reveal founder effects across geographical regions, *PeerJ* (2020). DOI: 10.7717/peerj.9255