

# Sequencing respiratory viruses provides new insight on coinfections, viral spread and COVID

November 1 2021

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Dr. Ravindra Kolhe. Credit: Michael Holahan, Augusta University

With mask wearing and social distancing on the decline and the cold and flu season upon us, researchers have developed a viral panel that enables

the simultaneous testing for SARS-CoV-2 along with numerous common respiratory viruses, that tells us whether other viruses also are at play in patients hard hit by COVID.

This new genetic epidemiology tool that provides detailed genetic information about the viruses present when packaged with a molecular immunology model called Nextstrain also enables researchers to assess the novel viral variants that are circulating in a state or nation and patterns for their spread with the goal of helping predict and mitigate future outbreaks, says Dr. Ravindra Kolhe, director of the Georgia Esoteric and Molecular Laboratory, or GEM Lab, at the Medical College of Georgia at Augusta University.

Deficits in SARS-CoV-2 monitoring and keeping tabs on other co-circulating respiratory viruses have been public health challenges during the pandemic, Kolhe and his colleagues report in the journal *Viruses*.

Coinfection is a reality, Kolhe says with these respiratory viruses that we unwittingly transmit through the air when we cough, sneeze, even talk, particularly when we are in close quarters for long periods like hospitals, nursing homes, schools and potentially even our workplace.

Another reality is that coinfections can have the compounding effect of worsening symptoms and outcomes, much as we have all heard that co-morbid conditions like diabetes and hypertension can do, he says.

Particularly when patients are not doing well, looking for other respiratory viruses with the new panel could help provide insight on why and possibly new directions on how to help, he says. The more expansive panel is more expensive than straight COVID testing, which will remain the frontline test in this pandemic, Kolhe predicts.

While the cold and [flu season](#) were essentially a wash last year because

of COVID precautions like mask wearing—in fact the coinfection rate in the group they studied was under 1%—he and others are concerned the cold and flu season now upon us will be very different even with vaccination initiatives for both COVID and the flu.

"We are concerned that because most of us are no longer wearing masks or social distancing and have mostly resumed our normal schedules that one consequence will be more coinfections," Kolhe says. "We feel this is a good tool to have ready when the flu and cold season hit."

Working with the San Diego-based biotech firm [Illumina](#), the researchers developed a 41-[virus](#) panel that includes four common human coronaviruses that have been causing colds in people for years as well as SARS-CoV-2, and other players like RSV, [respiratory syncytial virus](#), which also causes a typically mild cold, and more than a dozen influenza viruses.

They looked at 483 patient samples, mostly taken by nasopharyngeal swab, as well as a dozen saliva samples, that had tested positive for SARS-CoV-2 from across the state of Georgia between June 2020 and the end of December.

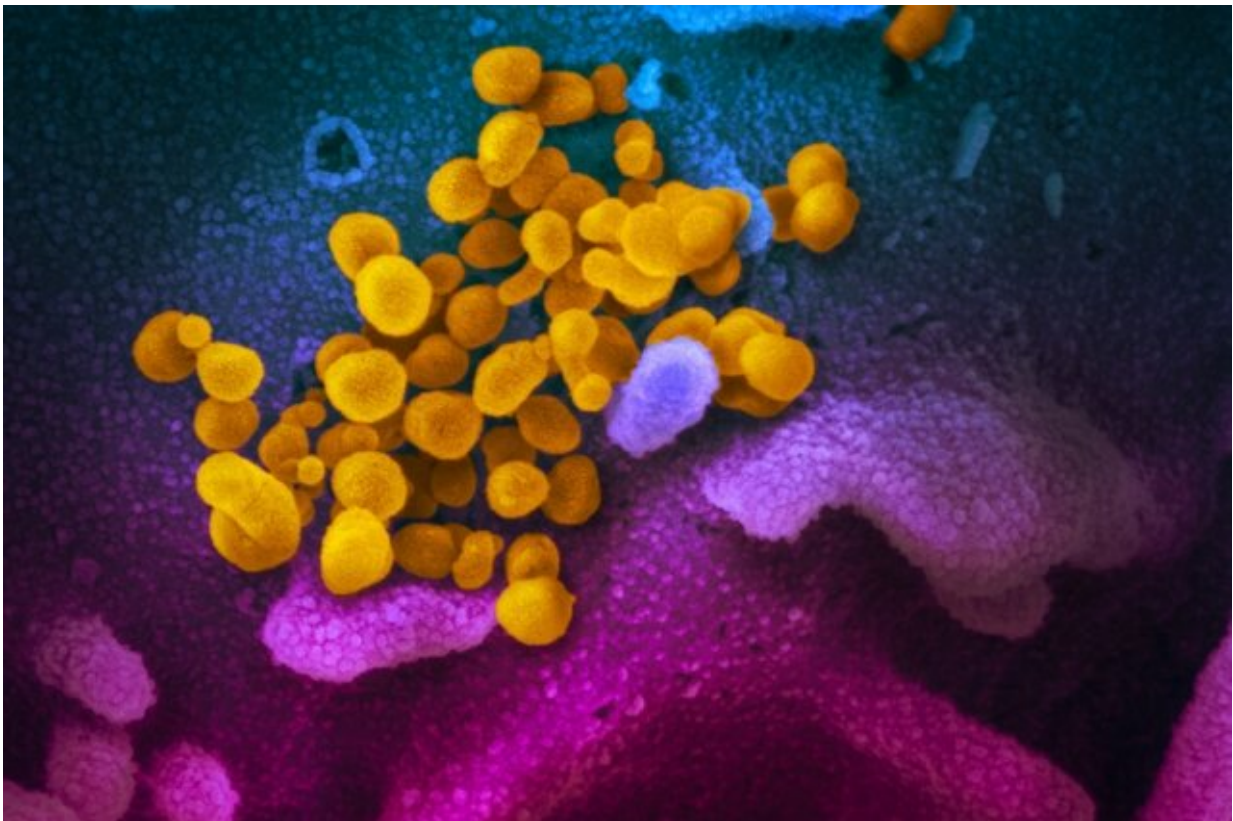
Standard SARS-CoV-2 testing uses polymerase chain reaction, or PCR, which can tell you if the virus is present, but the technique they are using for the panel actually sequences the viral genome enabling detection of variants, like the potential more deadly Delta variant, that have made headlines in recent months.

It also details changes in the larger, conserved region of the virus that occur essentially every time it multiplies, which indicates it has found a host organism, like a human. While those small changes in the conserved region of the virus don't impact clinical outcome, they do provide a sort of genomic stamp of where the virus came from, Kolhe says, as he

watches their interactive visualization of an individual in Augusta with 10 distinct but benign changes in the conserved region, changes that show up next in about 100 infected people in Savannah.

"There is no molecular coincidence that the exact same sequence is going to show up in Savannah," he says. "This is a way to identify the starting point, watch how people's movement actually moves the virus with them and which counties are going to be affected."

The unique molecular signature also is a way to know which cases are not connected. One of the questions he wants to answer is when this iteration of the virus infects another person does it experience more of these changes.



This scanning electron microscope image shows SARS-CoV-2 (yellow)—also known as 2019-nCoV, the virus that causes COVID-19—isolated from a patient, emerging from the surface of cells (blue/pink) cultured in the lab. Credit: NIAID-RML

The interactive visualization model they use to watch viral spread play out can also track the movement of variants, like Delta, that do have direct clinical consequences like degree of contagiousness and resulting sickness.

Kolhe notes that some of the human movement may happen before the individual realizes he is positive.

Knowing precisely which viruses are present is important because, while there is some commonality among the respiratory viruses, the treatments tend to be different, but there is not much crossover data on how much to date, Kolhe says. As examples, what happens if a patient with COVID-19 who is coinfecting with a flu virus, gets treated with monoclonal antibodies, manmade antibodies that target the virus, or corticosteroids that help reduce the hyper-immune response that can destroy the lungs in a process called a cytokine storm. There is some evidence that monoclonal antibodies and corticosteroids may also be effective for some flu but many questions remain, like what happens when the [monoclonal antibodies](#) are made specifically for the COVID virus. There is some evidence that vaccines for flu and COVID don't appear to have an overlap in protection.

Respiratory viruses are known to be present in pairs, for example the common rhinovirus in conjunction with another cause of the common cold, including some other common coronaviruses, can heighten related misery like a runny nose, headache and cough, according to the Centers



for Disease Control and Prevention.

Also, while you can be tested for the virus responsible for your flu, many times patients are not tested and SARS-CoV-2—along with what appears to be one of the mildest cold and flu seasons since current data reporting systems were initiated in 1997—has further decreased the chance of that happening in recent times, Kolhe says.

Stanford University reported in late March 2020 that about 1 in 5 people with COVID-19 were also infected with other [respiratory viruses](#) and that 1 in 10 people with symptoms of respiratory illness diagnosed with a common respiratory virus also were co-infected with the COVID-19 virus, SARS-CoV-2. Coinfections bacteria and fungi also occur.

While a lot has been learned about SARS-CoV-2 in the past nearly two years, there is insufficient documentation of the variations in the genome of the virus, some of which contribute to how the virus acts, and little insight on other viruses coinfecting people, Kolhe says.

The new study shows that genomic epidemiology is essential in predicting [disease transmission](#) and patterns of transmission, including the potential to recognize a likely resurgence, the investigators write.

Their findings included identifying which version of the virus was most prevalent early in the pandemic in Georgia: The clade for pangolin lineage B.

Co-authors on the study include flu expert Dr. Ted Ross, director of the Center for Vaccines and Immunology and Georgia Research Alliance Eminent Scholar and professor of infectious diseases at the University of Georgia, and Dr. Justin Bahl, an associate professor in the center with expertise in disease ecology, modeling and infectious diseases and virology. Ross is leading one of the new Collaborative Influenza Vaccine

Innovation Centers, a National Institutes of Health-funded initiative to develop a single dose vaccine that can protect against multiple strains of the flu virus.

Respiratory viruses can be spread by touch, like shaking hands or touching a surface where the virus is present then touching your nose, mouth or eyes, the CDC says. Both the cold and flu viruses are essentially always present but the fall and winter are generally considered flu season and late August through early Spring is the prime time for colds, the CDC says. And, those with underlying health conditions, who are older or pregnant are considered at higher risk for serious illness and complications from both COVID-19 and the flu.

Nextstrain is routinely used by the CDC to better predict what the flu viruses will look like in an upcoming season, so the vaccines can better target them, and likely areas of major impact.

The panel Kolhe and his colleagues developed already is available to other researchers through Illumina. The process of validation of the panel's efficacy also is available.

**More information:** Nikhil S. Sahajpal et al, High-Throughput Next-Generation Sequencing Respiratory Viral Panel: A Diagnostic and Epidemiologic Tool for SARS-CoV-2 and Other Viruses, *Viruses* (2021). [DOI: 10.3390/v13102063](https://doi.org/10.3390/v13102063)

Provided by Medical College of Georgia at Augusta University

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