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COVID-19 Molecular Virology

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Molecular Virology

SARS-CoV-2, the virus that causes COVID-19, is a large, single stranded RNA virus in the family of coronaviruses. After emerging in human populations in late 2019, SARS-CoV-2 has spread worldwide leading to millions of infections and hundreds of thousands of deaths. After entering the cell via the host's ACE2 receptor, SARS-CoV-2 can infect a wide range of cells, including in the patient's lungs, leading to problems breathing and pneumonia.

Shortly after the discovery of COVID-19 cases in China, molecular biologists sequenced the full viral genome, identified the host receptor in cell culture, and described both serology (antibody) and RNA-based (PCR) tests for SARS-CoV-2 infection.

These molecular studies of SARS-CoV-2 have been essential for our public health professionals to respond to the COVID-19 pandemic. We call for ongoing tight collaboration between public health officials and clinical labs with access to SARS-CoV-2 samples, and academic researchers with molecular virology expertise.

Viral RNA Sequencing

The SARS-CoV-2 viral replication machinery, like that of other coronaviruses, encodes an error checking domain. Therefore, its mutation rate is slow compared to other RNA viruses, like HIV and influenza.

A large-scale, global project sequenced the viral RNA of thousands of samples to determine the number and position of mutations (single nucleotide polymorphisms or SNPs) from the inferred ancestral virus that was present in China in late 2019. A map of viral relatedness, or phylogeny, can then be built that shows the evolutionary trajectory of viral spread.

This research allows researchers 1) to infer the number of ongoing infections and clusters through mechanisms that are less accurate than classical epidemiology but importantly that do not rely on wide scale testing; 2) to rapidly determine whether there is evidence of viral evolution and the emergence of new strains or mutations that become more common in the population; 3) to determine whether a new infection in a known outbreak center is due to community spread or re-introduction from another location.

Viral RNA sequencing and Infectivity Assays

The most widely used tests for SARS-CoV-2 infection use a qPCR method to amplify the viral RNA. Research has clearly demonstrated that the viral RNA can be present in samples, and on surfaces, where no infectious virus exists. Therefore, while qPCR testing is a sensitive method to determine whether an individual has recently been infected with SARS-CoV-2, it does not indicate whether that individual is currently infectious. Nor does positive samples for viral RNA on surfaces or in the air indicate the presence of infectious virus.

Researchers must continue to determine not the RNA-positivity of samples from patients and surfaces, but the ability to recover infectious virus as determined by viral culture. These questions are fundamental to our understanding of when individuals can leave quarantine after a positive test, how long viral particles exist on various surfaces, and how long SARS-CoV-2 remains infectious in the air.