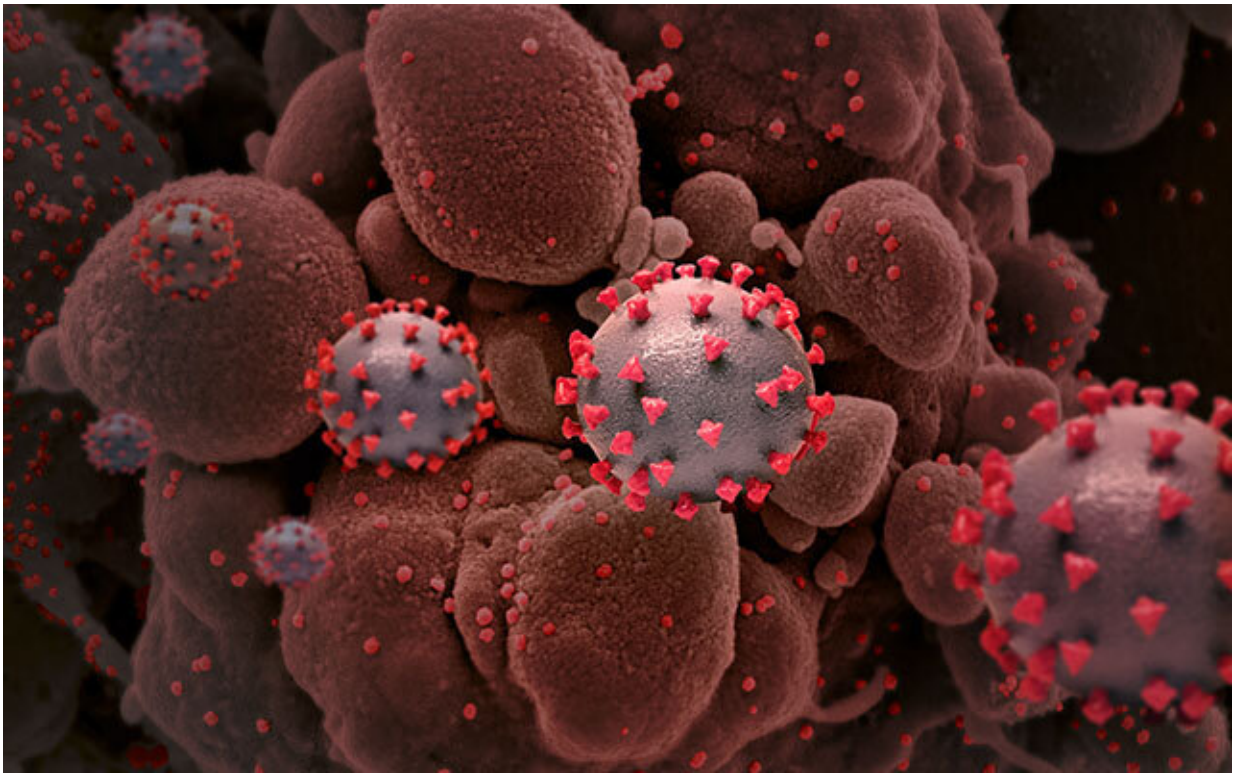
Study finds genetic markers may predict severity of COVID-19 infection

October 26 2021



Creative rendition of SARS-CoV-2 particles (not to scale). Credit: National Institute of Allergy and Infectious Diseases, NIH

Scientists at the University of Colorado School of Medicine, along with colleagues at UCHealth University of Colorado Hospital, have discovered specific genetic biomarkers that not only show who is

infected with COVID-19, but offer insights into how severe the disease might be, filling a major diagnostic gap.

"I think this study is a tremendous proof-of-concept in the realm of COVID-19 testing, one that can be applied to other diseases," said the study's lead author, Kathleen Barnes, Ph.D., professor at the CU School of Medicine. "It's a major move forward in the world of precision medicine."

The study, published Tuesday in the journal *Communications Medicine*, suggests that specific signals from a process called DNA methylation varies between those infected and those not infected with SARS-CoV-2. And they can indicate the severity of the disease even in the early stages.

DNA methylation, critical in how cells function, is an epigenetic signaling tool that cells use to turn genes off. Any mistakes in the process can trigger a variety of disease.

Barnes believes that paying attention to these signals could help fill a needed gap in the current world of COVID testing. Most COVID-19 antigen or rapid tests are dependent on viral strains and can carry high false negative rates. They don't predict if the virus is viable and replicating, nor do they predict clinical outcomes, the study said.

A pre-symptomatic patient may test negative for the SARS-CoV-2 virus while patients who have recovered may still test positive despite no longer being infectious.

"Accurate diagnostics are urgently required to control continued communal spread, to better understand host response, and for the development of vaccines and antivirals," the study said. "Identification of which SARS-CoV-2 infected patients are most likely to develop severe disease would enable clinicians to triage patients via augmented

clinical decision support."

But the authors said they didn't know of any test that can predict the clinical course of COVID-19.

With that in mind, they analyzed the epigenome in blood samples from people with and without COVID-19. They customized a tool from Illumina called the Infinium Methylation EPIC array to enhance immune response detection. Researchers then profiled peripheral blood samples from 164 COVID-19 patients and 296 control patients.

The peripheral blood DNA samples were collected from patients seen at UCHealth and tested for SARS-CoV-2 epigenetic signatures starting March 1, 2020. Most blood specimens were collected in the University of Colorado Emergency Medicine Specimen Bank under the direction of study co-author Andrew Monte, MD, Ph.D., and passed on to the Colorado Anschutz Research Genetics Organization (CARGO). Additional specimens were taken from patients consented to the University of Colorado COVID-19 Biorepository.

The researchers discovered specific genetic markers of SARS-CoV-2 infection along with indications of how severe the disease might be.

"These signals of disease progression were present from the initial blood draw when first walking into the hospital," the study said. "Together, these approaches demonstrate the potential of measuring the epigenome for monitoring SARS-CoV-2 status and severity."

According to Barnes, the findings could ultimately lead to a new and more accurate way to test for COVID-19.

"We are exploring how this platform could add value to the COVID diagnostic world," she said. "We think it adds value to knowing what

patients develop more serious disease. This could tell you if you could ride out the infection or if it is likely to get worse."

More information: Iain R. Konigsberg et al, Host methylation predicts SARS-CoV-2 infection and clinical outcome, *Communications Medicine* (2021). DOI: 10.1038/s43856-021-00042-y

Provided by CU Anschutz Medical Campus