Biomarkers could be used in a quick, inexpensive COVID-19 blood screening tool

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Dr. Douglas Fraser, Researcher from Lawson Health Research Institute and Western University's Schulich School of Medicine & Dentistry Credit: Lawson Health Research Institute

A new study from Lawson Health Research Institute, Western University

and University of Alberta suggests that COVID-19 affects the human body's blood concentration levels of specific metabolites—small molecules broken down in the human body through the process of metabolism. Three specific metabolites identified in this study could act as biomarkers and one day be measured through an inexpensive blood test to quickly screen patients for the disease and predict which patients will become most critically ill. The team also suspects those metabolites depleted by the virus could be delivered to patients as dietary supplements, acting as a secondary therapy. Published in *Critical Care Explorations*, the early findings add to the research team's growing body of evidence on the bodily changes caused by the SARS-CoV-2 virus.

"As the second wave progresses and COVID-19 cases rise, there is an overwhelming demand for testing," says Dr. Douglas Fraser, lead researcher from Lawson and Western's Schulich School of Medicine & Dentistry, and Critical Care Physician at London Health Sciences Centre (LHSC). "While our findings need to be confirmed in a larger group of patients, they could lead to a rapid, cost-effective screening tool as a first line of testing in the community and in-hospital."

The study was conducted by performing metabolomics profiling on blood samples from 30 participants at LHSC: 10 COVID-19 patients and 10 patients with other infections admitted to LHSC's ICU, as well as 10 healthy control participants. Samples were sent to The Metabolomics Innovation Centre (TMIC) at University of Alberta where a team measured plasma concentrations of 162 metabolites.

"Metabolites are the final breakdown products in the human body and play key roles in cellular activity and physiology. By studying them, we can understand chemical processes that are occurring at any given moment, including those that regulate biological functions related to health and disease," explains Dr. David Wishart, Codirector of TMIC and Professor of Biological Sciences, Computing Science and

Laboratory Medicine & Pathology with the University of Alberta. "Because the human metabolome responds very quickly to environmental factors like pathogens, metabolomics can play an important role in early-stage disease detection, including for COVID-19."

The team discovered four metabolites of importance to COVID-19 disease detection. The concentration of one metabolite called kynurenine was elevated in COVID-19 patients while concentrations of the other three metabolites (arginine, sarcosine and lysophosphatidylcholines) were decreased. After further analysis, they discovered that by studying the concentrations of only two metabolites—kynurenine and arginine—they could distinguish COVID-19 patients from healthy participants and other critically ill patients with 98 per cent accuracy.

The team also discovered that concentrations of two metabolites (creatinine and arginine) could be used to predict which critically-ill COVID-19 patients were most at risk of dying. When measured on a patient's first and third day in ICU, these metabolites predicted COVID-19-associated death with 100 per cent accuracy.

"It's our hope these findings can be validated in larger patient populations and then used to develop a simple blood test that shows high likelihood of infection and disease severity, providing rapid results in as little as 20 minutes," explains Dr. Fraser. "This could ease the demand for current testing methods, perhaps being used as a portable, first-line screening tool in the community and for when undiagnosed patients present to hospital."

The team also notes the reduction of key metabolites reflects changes to biochemical pathways or functions in the body which are important to maintaining health and fighting disease. They suggest their findings warrant further study to determine whether certain metabolites could be

boosted through dietary supplements. A precision health approach like this could lead to repaired biochemical pathways and improved disease outcomes.

"Providing dietary supplements could be a simple adjunctive or secondary therapy with meaningful outcomes," says Dr. Fraser. "For example, the metabolite arginine is essential to tissue repair while the metabolite sarcosine activates a process to remove damaged cells. Knowing that COVID-19 causes hyperinflammation that can damage cells and tissue, particularly in the lungs, supporting these processes may prove critical."

In an earlier study, the team was the first to profile the body's immune response to the SARS-CoV-2 virus and discover six potential therapeutic targets to improve outcomes. In other studies, they have discovered additional biomarkers that could be used to predict how severely ill a COVID-19 patient will become and uncovered a mechanism causing blood clots in COVID-19 patients and potential ways to treat them.

"We're working to uncover hard evidence about how the virus invades the body. Ultimately, we hope our combined findings can lead to faster diagnosis, ways to identify patients most at risk of poor outcomes and targets for novel treatments," notes Dr. Fraser.

More information: Douglas D. Fraser et al, Metabolomics Profiling of Critically Ill Coronavirus Disease 2019 Patients: Identification of Diagnostic and Prognostic Biomarkers, *Critical Care Explorations* (2020). DOI: 10.1097/CCE.0000000000000272

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