New insights into how patient factors and COVID-19 infection affect antibody responses in people with HIV

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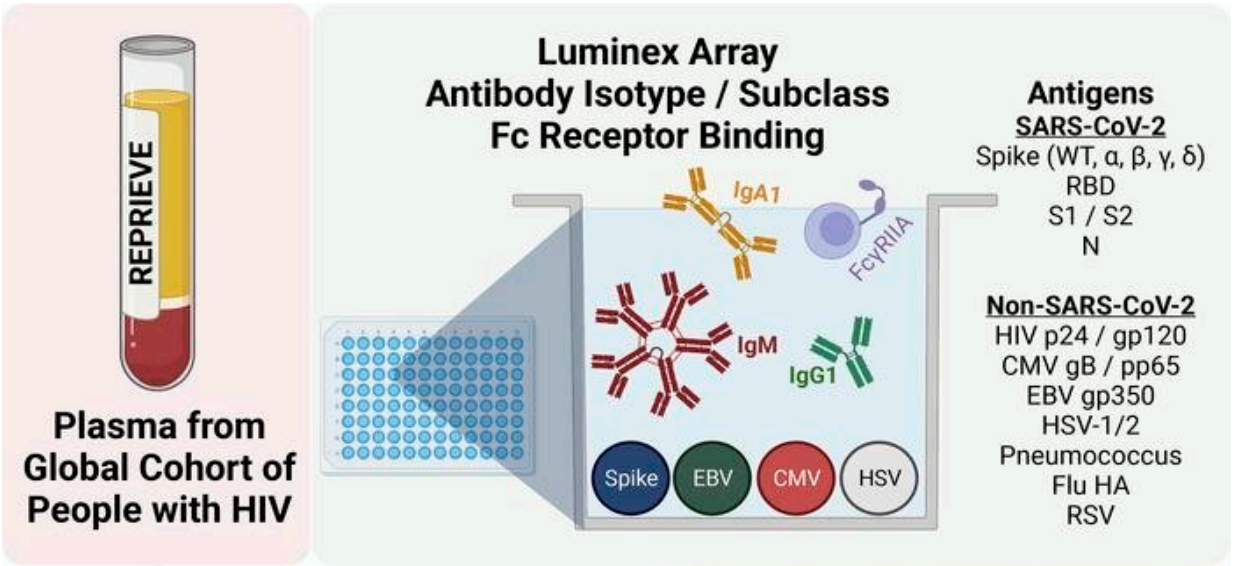
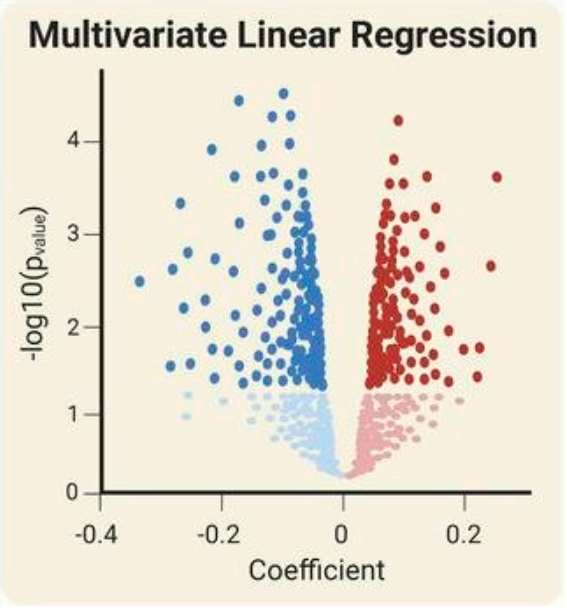


Cohort	Effect of	Humoral Repertoire: SARS-CoV-2	Humoral Repertoire: Non-CoV-2
Full	COVID-19	↑ Repertoire	↑ CMV ↑ EBV
COVID Ab +	COVID-19 Severity & Host Factors	↑ COVID-19 Severity ↑ BMI ↑ Lower nadir CD4	No Effect of COVID-19 Severity
COVID Ab -	Host Factors	N/A	↑ High-income Region ↑ Female Sex ↑ Age ↑ Lower nadir/ current CD4 ↑ HIV Viremia



Credit: *JCI Insight* (2023). DOI: 10.1172/jci.insight.166848

People with HIV have impaired immune responses to some pathogens and immunizations, and during the COVID-19 pandemic, they often experienced severe symptoms if infected with SARS-CoV-2. New research led by investigators at Massachusetts General Hospital (MGH) has examined how patient characteristics and COVID-19 infection may affect the antibody responses of people with HIV—including antibody responses against SARS-CoV-2 proteins as well as proteins from other viruses such as cytomegalovirus (CMV) and Epstein-Barr Virus (EBV).

The study, which is published in *JCI Insight*, involved data from the global Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE), a large ongoing cardiovascular prevention trial testing the effects of statins in people with HIV on antiretroviral therapy that has collected information related to COVID-19 diagnoses, symptoms, and adverse events every four months starting in April 2020. (Participants vaccinated against SARS-CoV-2 were excluded.) Investigators also used a novel platform to assess the various types of non-SARS-CoV-2 and SARS-CoV-2 antibodies present in 2,464 participants' blood.

"We asked whether COVID-19 infection impacted the antibody response to non-SARS-CoV-2 proteins—in this case proteins from CMV and EBV. We also asked what is the effect of host factors on SARS-CoV-2 antibody responses among COVID-positive participants," says senior author Steven Grinspoon, MD, chief of the MGH Metabolism Unit and director of the Nutrition Obesity Research Center at Harvard.

In the overall analysis, COVID-19 infection was associated with higher CMV and EBV antibody responses. Among COVID-positive

participants, higher body mass index was associated with an amplified SARS-CoV-2 response, and lower nadir CD4+ T-cell count (a person's lowest CD4+ T-cell count) was associated with an ineffective or poorly functional antibody response to SARS-CoV-2.

"The higher EBV and CMV responses in those with COVID-19 may signify increased susceptibility to or be a consequence of persistent inflammation, and the abnormal repertoire seen among those with obesity could portend an increased inflammatory response in this group," says Grinspoon. "The connection to nadir CD4 and increased immune response to COVID was interesting as nadir CD4 is a marker of immune function and suggests a key linkage between HIV-related immune function and abnormal COVID immune responses."

As the REPRIEVE trial continues and generates data related to the effects of statins on the acquisition and severity of COVID-19 and long COVID in people with HIV, Grinspoon and his colleagues anticipate that their novel antibody platform may provide new mechanistic insights into the short- and long-term complications of SARS-CoV-2 infection.

More information: Samuel R. Schnittman et al, Effect of host factors and COVID-19 infection on the humoral immune repertoire in treated HIV, *JCI Insight* (2023). DOI: 10.1172/jci.insight.166848

Provided by Massachusetts General Hospital