RESEARCH

‘Immune Distraction’ from Previous Colds Leads to Worse COVID Infections

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At the beginning of the COVID pandemic, we were hopeful that pre-existing immunity to the common cold could protect you from COVID, but new evidence suggests that sometimes the opposite can happen. A new University of Rochester Medical Center study shows that prior infection and immunity to one of the common cold coronaviruses may have put people at risk of more severe COVID illness and death.

The study, published in the *Journal of Infectious Diseases*, examined immunity to various coronaviruses, including the COVID-causing SARS-CoV-2 virus, in blood samples taken from 155 COVID patients in the early months of the pandemic. Of those patients, 112 were hospitalized and provided sequential samples over the course of their hospitalization. These hospitalized patients experienced a large, rapid increase in antibodies that targeted SARS-CoV-2 and several other coronaviruses. While big boosts in antibodies – protective proteins generated by the immune system – is usually a good thing, in this case, it wasn’t.

The study showed that these antibodies were targeting parts of the spike protein (which sits on the surface of coronaviruses and helps them infect cells) that were similar to common cold coronaviruses the immune system remembered from previous infections. Unfortunately, targeting those areas meant the antibodies could not neutralize the new SARS-CoV-2 virus. When levels of these antibodies rose faster than levels of SARS-CoV-2 neutralizing antibodies, patients had worse disease and a higher chance of death.

“In people who were sicker – those who were in the ICU or died in the hospital, the immune system was responding robustly in a way that was less protective,” said lead study author Martin Zand, M.D., Ph.D., who is the senior associate dean of Clinical Research at URMC. “It took those patients longer for the immune system to make protective antibodies… unfortunately, too late for some.”

This study adds to a growing pool of evidence that a phenomenon called immune imprinting is at play in COVID immune responses. Zand, who is also a co-director of the University of Rochester Clinical and Translational Science Institute (UR CTSI), likens this phenomenon to ‘immune distraction’: immunity to one threat (seasonal coronaviruses) hijacks the immune response to a new, but similar threat (SARS-CoV-2). Immune imprinting has been linked to poor immune responses to other viruses, like flu, and can have implications for vaccine strategies.

By some predictions, COVID is likely to be with us for a long time – with new, milder strains emerging and circulating on an annual or seasonal basis. If those predictions hold true, the study suggests that we will need to regularly develop new vaccines targeting the new strains of SARS-CoV-2. While none have come to market yet, pharmaceutical companies like Pfizer and Moderna have been developing and testing new versions of their COVID vaccines as new variants of concern have emerged.

“We should expect that development of new vaccines is a good thing," said Zand. "It doesn’t mean the original science was wrong. It means nature has changed. If we want an immune system that pays attention to the right stuff, we need to teach it new tricks with different vaccines.”

The study also analyzed 188 blood samples collected in the pre-COVID era (prior to December of 2019) as controls. Some of the blood samples analyzed for the study were provided by the UR CTSI’s COVID-19 Biobank, a repository of blood samples from hundreds of patients with and without COVID infections that was developed by the UR CTSI and URMC Shared Resource Labs.

The following URMC researchers also contributed to this study: Jiong Wang, B.Med., M.S., Dongmei Li, Ph.D., Andrew Cameron, Ph.D., Qian Zhou, B.M., M.S., Alexander Wiltse, Jennifer Nayak, M.D., and Nicole Pecora.

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