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CONTACT: Caree Vander Linden
(301) 619-2285
teresa.l.vanderlinden.civ@mail.mil

Army and Illinois Researchers Design, Test Protein that May Lead to COVID-19 Therapeutic

A novel receptor protein that binds to the SARS-CoV-2 virus and prevents it from entering cells may hold promise for treating COVID-19 and other coronavirus-related diseases, according to research published online Aug. 4 in the journal SCIENCE.

As scientists race to find treatments for COVID-19, many are focused on a specific protein called angiotensin-converting enzyme 2, or ACE2, which is found on various cell surfaces throughout the human body. Its purpose is to generate smaller proteins that regulate functions within the cell. Using the spike-like protein on its surface, the SARS-CoV-2 virus binds to ACE2 prior to entry and infection of cells. Thus, ACE2 acts as a receptor for the virus that causes COVID-19.

In the study, Dr. Erik Procko and scientists at the University of Illinois engineered a novel receptor that resembles ACE2, with the intent of using it as a "decoy" that can bind to the virus before it can latch onto ACE2 at the cell surface and invade the cell. First, Procko examined more than 2,000 ACE2 mutations and created cells with the mutant receptors on their surfaces. By analyzing how these interacted with the coronavirus spike protein, he found a combination of three mutations that made a receptor that bound to the virus more strongly and made it a more "attractive" target for the virus.

After Procko posted his findings to a preprint server, a colleague connected him with the U.S. Army Medical Research Institute of Infectious Diseases. USAMRIID scientists, including Dr. Andrew Herbert of The Geneva Foundation, agreed to test the receptor in cells using live SARS-CoV-2.

"We were already in the process of testing several therapeutic candidates for SARS-CoV-2, and Erik's approach seemed novel—and certainly compelling enough to give it a shot," commented Herbert.

USAMRIID's team determined that the decoy receptor has potent neutralizing activity against SARS-CoV-2, activity that is on par with the best neutralizing antibodies identified to date. Furthermore, they found that the decoy receptor not only neutralizes SARS-CoV-2, but also acts to neutralize SARS-CoV-1, a closely related virus that uses the same cellular receptor.

"Once we confirmed neutralizing activity against SARS-CoV-2, it made sense to test for pan-coronavirus activity against other coronaviruses that also use ACE2 to enter cells," said Herbert.

Additional research is required to determine whether the decoy receptor could be used to effectively treat or prevent COVID-19 and related coronavirus diseases, according to Herbert. The team hopes to secure funding for animal studies to help answer those questions.

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About the U.S. Army Medical Research Institute of Infectious Diseases:

For over 50 years, USAMRIID has provided leading edge medical capabilities to deter and defend against current and emerging biological threat agents. The Institute is the only laboratory in the Department of Defense equipped to safely study highly hazardous viruses requiring maximum containment at Biosafety Level 4. Research conducted at USAMRIID leads to medical solutions – vaccines, drugs, diagnostics, information, and training programs – that benefit both military personnel and civilians. Established in 1969, the Institute plays a key role as the lead military medical research laboratory for the Defense Threat Reduction Agency's Joint Science and Technology Office for Chemical and Biological Defense. USAMRIID is a subordinate laboratory of the U.S. Army Medical Research and Development Command. For more information, visit www.usamriid.army.mil.

Reference:

Engineering human ACE2 to optimize binding to the spike protein of SARS coronavirus 2; DOI: 10.1126/science.abc0870. https://science.sciencemag.org/content/early/2020/08/03/science.abc0870

Authors:

Kui K. Chan, Orthogonal Biologics; Danielle Dorosky, Shawn Abbasi, and John Dye, USAMRIID; Andrew Herbert, The Geneva Foundation at USAMRIID; and Preeti Sharma, David M. Kranz, and Erik Procko, University of Illinois.

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