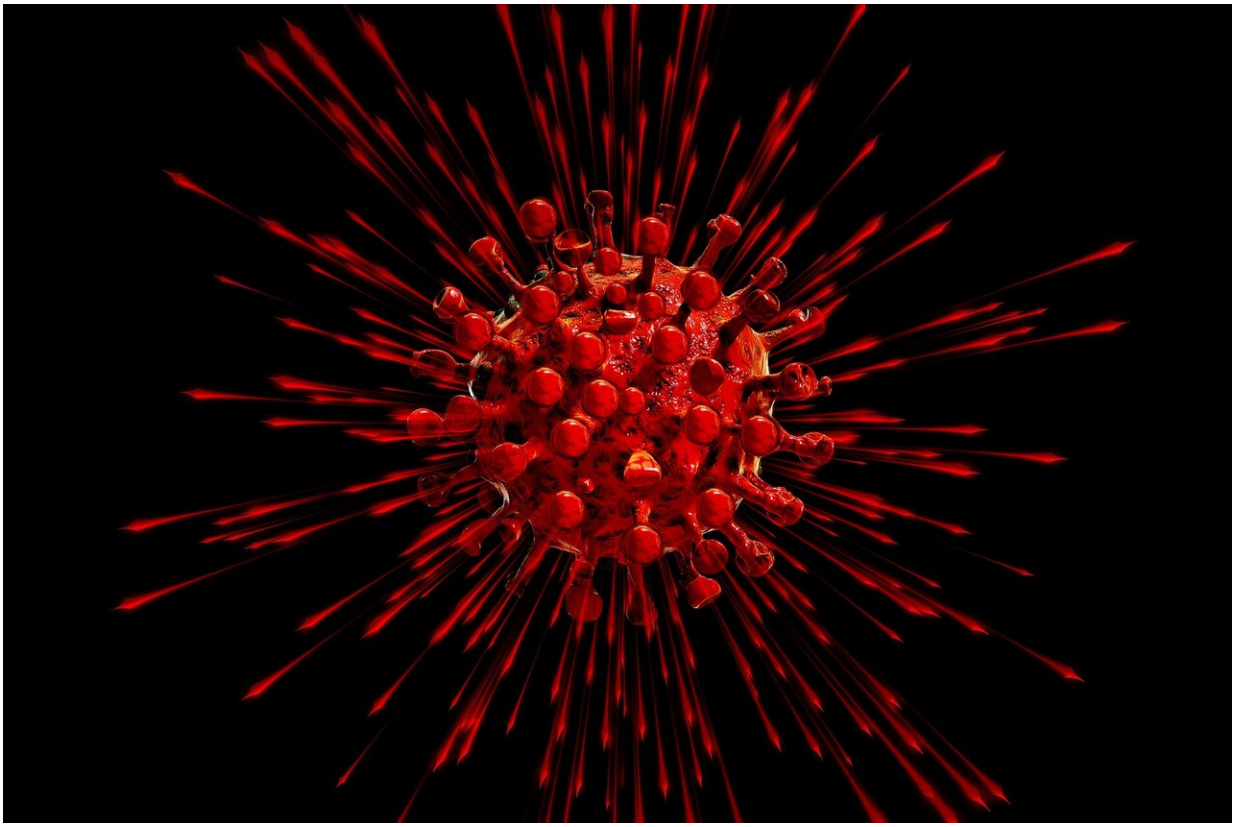
RCSI begins clinical trial for potential drug therapy for severe COVID-19 infection

June 29 2020



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Clinician scientists at RCSI University of Medicine and Health Sciences have begun a clinical trial of a promising therapy for critically ill COVID-19 patients in intensive care.

In a paper published in the *American Journal of Respiratory and Critical Care Medicine*, the team, led by RCSI Professors Gerry McElvaney and Ger Curley, describe changes in the body's normal inflammatory response in patients infected with COVID-19, in particular among those who require admission to intensive care.

The team has begun a randomised double blind placebo controlled clinical trial of alpha-1-antitrypsin to treat critically ill patients mechanically ventilated in ICU with COVID-19 associated Acute Respiratory Distress Syndrome. Alpha-1-antitrypsin is a naturally occurring human protein produced by the liver and released into the bloodstream which normally acts to protect the lungs from the destructive actions of common illnesses.

RCSI Professor of Medicine Prof. Gerry McElvaney said: "As of late June, more than 9.5 million laboratory-confirmed cases of COVID-19 have been documented globally, with over 490,000 deaths. These numbers continue to grow substantially. In Beaumont Hospital, we have had over 500 patients admitted to the hospital, and nearly 50 patients requiring admission to intensive care.

"The current management of severe COVID-19 remains supportive, focusing on supplemental oxygen and ventilator support in the event of acute respiratory failure. Despite the implications for global health, the inflammatory characteristics of patients with COVID-19 are not yet fully understood. A greater understanding of how the body's inflammatory mechanisms are impacted upon by COVID-19 could open the door to several potential therapies including antiviral medications and targeted immune-modulators such as alpha-1-antitrypsin."

Prof. Ger Curley, RCSI Professor of Anaesthesia and Critical Care and Consultant in Anaesthesia and Intensive Care in Beaumont Hospital explained that "we know from in-hospital studies that many COVID-19

patients in ICU develop severe inflammation throughout the body with a disproportionately high rate of progression to acute respiratory distress syndrome, acute renal failure, shock and heart arrhythmia."

In a collaboration between the Departments of Medicine and Critical Care and Anaesthesia, a team of clinician scientists led by Prof. McElvaney and Prof. Curley sought to ascertain the type of inflammation affecting the COVID-19 patient in ICU, and to determine whether there was a relationship between this type of inflammation and the need for intubation and mechanical ventilation.

The study showed that a number of highly inflamed proteins were all increased in infected patients compared to healthy controls. There was also a difference in the profiles of patients in ICU and those who were infected but stable.

Prof. Curley explained, however, that the most unanticipated differentiating factor between patients with stable and severe disease was not the degree of increase in inflammatory proteins, but rather the relative decrease in levels of an anti-inflammatory protein which indicates that the patients' anti-inflammatory mechanisms were failing.

"This finding suggests to us that a therapy which augments the body's own inflammation resolving mechanisms might have a positive impact. Alpha-1 protects the airway from damage during acute pulmonary infection. It is also a potent anti-inflammatory and acts to protect the immune system. Of particular relevance to COVID-19, it has been shown to modulate the production and activity of several key pro-inflammatory proteins", explained Prof. Curley.

"We are confident that this clinical trial will demonstrate the potential for Alpha-1 to improve the outcomes for patients with the most severe COVID-19 induced respiratory difficulties."

This is the first Investigational Medicine Product trial to be approved in Ireland to test a therapy to treat COVID19. The trial is being sponsored by RCSI University of Medicine and Health Sciences and is coordinated by the RCSI Clinical Research Centre. Beaumont Hospital is the first site to recruit patients and other sites in Ireland will also participate. This investigator initiated study benefited from generous support from Grifols, a Barcelona-based multinational healthcare company and a leading global producer of plasma-derived medicines, which provided access to the alpha1-proteinase inhibitor study drug.

Ranked number one globally for Good Health and Well-being in the Times Higher Education (THE) University Impact Rankings 2020, RCSI University of Medicine and Health Sciences is an international not-for-profit university, with its headquarters in Dublin.

RCSI is exclusively focused on education and research to drive improvements in human health worldwide. It is among the top 250 universities worldwide in the THE World University Rankings (2020) and its research is ranked first in Ireland for citations. RCSI has been awarded Athena Swan Bronze accreditation for positive gender practice in higher education.

More information: Oliver J McElvaney et al, Characterization of the Inflammatory Response to Severe COVID-19 Illness, *American Journal of Respiratory and Critical Care Medicine* (2020). DOI: 10.1164/rccm.202005-1583OC

Provided by RCSI

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