THE UNIVERSITY of EDINBURGH

Press Release

Issued: **8 July 2021**

UNDER STRICT EMBARGO until 16:00 BST 8 July 2021

Genetic variations linked to severe Covid-19 risk identified

An international group of scientists have discovered 13 DNA sequences that are associated with people developing the most severe form of Covid-19.

The identification of the sequences – known as genetic markers – could provide targets for future therapies using repurposed drugs, experts say.

Researchers from the University of Edinburgh joined a global effort to compare the genetic information of almost 50,000 Covid-19 patients with samples provided by healthy volunteers from biobanks, clinical studies, and direct-to-consumer genetic companies like 23andMe.

The team found key differences in 13 genetic markers of Covid-19 patients compared with healthy volunteers. The genes partially explain why some people become seriously ill with Covid-19, while others are not affected.

By pooling the large amount of data from 25 countries, the scientists were able to produce robust analyses more quickly, and from a greater diversity of populations, than any one group could have on its own.

The team also identified factors such as smoking and high body mass index as reasons why some people suffer from Covid-19 more acutely.

Of the 13 genetic markers identified so far, two occur more often among patients of East Asian or South Asian ancestry than in those of European ancestry.

One of these two markers, near the FOXP4 gene, is linked to lung cancer. The different FOXP4 sequence associated with severe Covid-19 increases the gene's expression, suggesting that inhibiting the gene could be a potential treatment strategy, experts say.

Other genetic markers associated with severe Covid-19 included DPP9, a gene also involved in lung cancer and pulmonary fibrosis, and the TYK2 gene, which is implicated in some autoimmune diseases.

The latest findings come from the COVID-19 Host Genomics Initiative, which have been published in Nature.

The initiative has grown to be one of the most extensive collaborations in human genetics and currently includes more than 3,300 researchers and 61 studies from 25 countries.

The University of Edinburgh led study GenOMICC (Genetics of Susceptibility and Mortality in Critical Care) is one such project that contributed data to the COVID-19 Host Genomics Initiative.

GenOMICC started in 2015 as an open, global consortium of intensive care clinicians dedicated to understanding genetic factors that influence outcomes in intensive care from diseases such as SARS, influenza and sepsis.

Throughout the pandemic it has been focused on Covid-19 research in partnership with Genomics England.

Researchers will continue to identify additional gene regions associated with infection and severe disease, and will begin to study what factors lead symptoms persisting in some patients for months.

GenOMICC is funded by the charity Sepsis Research FEAT, the Intensive Care Society, Wellcome, UK Research and Innovation, Scotland's Chief Scientist Office, the Department of Health and Social Care and the National Institute for Health Research.

Dr Kenneth Baillie, GenOMICC's chief investigator and Academic Consultant in Critical Care Medicine and Senior Research Fellow at University of Edinburgh's Roslin Institute, said: "By working together across the whole world, we are able to accelerate discovery for the benefit of patients. This new international analysis builds on the colossal effort made by patients and intensive care research teams across the whole UK in the GenOMICC study."

For further information, please contact: Shane Canning, Press and PR Office, 0755 782 0266, shane.canning@ed.ac.uk