PRESS RELEASE

THE HUMAN PROTEIN ATLAS

## What is the role of human protein ACE2 for SARS-CoV-2 infection of the human lung?

**Today, an article was published in bioRxiv (Hikmet et al) describing the presence in the human body of the enzyme Angiotensin I converting enzyme 2 (ACE2), previously suggested to be the main target for coronavirus attachment to the surface of human cells. The results raise questions regarding the role of ACE2 for infection of human lungs and highlights the need to further explore the route of transmission during SARS-CoV-2 infection.**

The international spread of the novel, pathogenic SARS-CoV-2, the agent of the COVID-19 disease, poses a global challenge on both healthcare and society. A multitude of research efforts worldwide aim at characterizing the cellular factors involved in viral transmission in order to reveal therapeutic targets. For a full understanding of the susceptibility for SARS-CoV-2 infection and the role of human receptors involved in host cell entry, it is necessary to study the cell type-specific expression of such receptors in human tissues, both on the mRNA and protein level. The respiratory system is of special interest due to its high susceptibility to inhaled viruses, however, it is also important to study other tissue locations that could serve as potential entry. When coronaviruses enter the target cell, a surface unit of the spike (S) glycoprotein binds to a cellular receptor. Upon entry, cellular proteases cleave the S protein which leads to fusion of the viral and cellular membranes. The severe acute respiratory syndrome coronavirus (SARS-CoV) that caused the SARS outbreak in 2002 has previously been shown to enter the cell via Angiotensin I converting enzyme 2 (ACE2), primed by the cellular serine protease TMPRSS2. The novel SARS-CoV-2 shares ~80% amino acid identity with SARS-CoV, and recent studies suggest that also SARS-CoV-2 employs ACE2 and TMPRSS2 for host cell entry.

Based on antibody-based data from the Tissue Atlas, part of the Human Protein Atlas program funded by Knut and Alice Wallenberg Foundation, the manuscript published today presents an overview of ACE2 expression in the entire human body and reviews the evidence for the presence of this protein in human lung. “Our analysis suggests that ACE2 is mainly located in the intestine, kidney, gallbladder, male reproductive organs and heart, while the expression in the human respiratory system appears to be limited”, says Dr Cecilia Lindskog, senior author on the paper and Head Director of the HPA Tissue Atlas team at Uppsala University. “The lack of ACE2 protein expression in human respiratory system raises questions regarding the role of ACE2 for infection of human lungs, and highlights the need to further explore the route of transmission during SARS-CoV-2 infection. This will aid in the development of effective treatments to the viral infection”, says Cecilia Lindskog

Many of the earlier studies have shown inconsistent and contradictory results, in particular protein studies using antibodies proposed to be specific for ACE2. “The HPA program has spent a considerable effort on introducing and implementing a new concept for enhanced validation of antibodies using strategies proposed by International Working Group for Antibody Validation (IWGAV), and the antibodies used in the HPA for immunohistochemical analysis of ACE2 have passed the criteria for enhanced antibody validation”, says Prof Mathias Uhlén, Director the HPA consortium and co-author on the paper. The results, including also transcriptomics, proteomics and single cell analysis, suggests that the expression of ACE2 in the human respiratory system appears to be limited, and the expression of the receptor in lung or respiratory epithelia on the protein level is yet to be confirmed.

Read the full article about ACE2: Hikmet et al (www.biorxiv.org/content/10.1101/2020.03.31.016048v1)

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**About**

**Human Protein Atlas**

The Human Protein Atlas (HPA) is a program based at the Science for Life Laboratory (Stockholm) and started in 2003 with the aim to map all of the human proteins in cells, tissues and organs using integration of various omics technologies, including antibody-based imaging, mass spectrometry-based proteomics, transcriptomics and systems biology. All the data in the knowledge resource is open access to allow scientists both in academia and industry to freely use the data for exploration of the human proteome. Version 19 consists of six separate parts, each focusing on a particular aspect of analysis of the human proteins: (i) the Tissue Atlas showing the distribution of the proteins across all major tissues and organs in the human body; (ii) the Cell Atlas showing the subcellular localization of proteins in single cells; (iii) the Pathology Atlas showing the impact of protein levels for survival of patients with cancer; (iv) the Blood Atlas showing the profiles of blood cells and proteins detectable in the blood; (v) the Brain Atlas showing the distribution of proteins in human, mouse and pig brain; and (vi) the Metabolic Atlas showing the presence of metabolic pathways across human tissues. The Human Protein Atlas program has already contributed to several thousands of publications in the field of human biology and disease and it has been selected by the organization ELIXIR (www.elixireurope.org) as a European core resource due to its fundamental importance for a wider life science community. The HPA consortium is funded by the Knut and Alice Wallenberg Foundation. For more information, see: www.proteinatlas.org

**Knut and Alice Wallenberg Foundation**

The Knut and Alice Wallenberg Foundation is the largest private financier of research in Sweden and also one of Europe's largest. The Foundation's aim is to benefit Sweden by supporting basic research and education, mainly in medicine, technology, and the natural sciences. The Foundation can also initiate grants to strategic projects and scholarship programs. For more information, see: kaw.wallenberg.org

**Uppsala University**

Uppsala University is the Nordic region's oldest university – founded in 1477 – and is ranked among the top 100 universities in the world. Uppsala University is divided into three disciplinary domains: humanities and social sciences, medicine and pharmacy, and science and technology. These in turn consist of nine faculties and nearly 50 departments in total. For more information, see: www.uu.se