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LEIBNIZ INSTITUTE FOR EXPERIMENTAL VIROLOGY (HPI)

Adipose tissue is an important SARS-CoV-2 replication site

Hamburg. Obesity is an important risk factor for severe disease progression in COVID-19 patients. A multidisciplinary research team from the Leibniz Institute for Experimental Virology (HPI) and the University Medical Center Hamburg-Eppendorf (UKE) has now demonstrated an important role of adipose tissue in the viral replication of SARS-CoV-2. The results, which also identify new therapeutic strategies for the treatment of SARS-CoV-2 infections, were published in the online edition of the renowned journal *Cell Metabolism*.

Globally, excessive body weight poses a serious threat to public health. According to the World Health Organization, the prevalence of obesity has increased dramatically in recent decades and has now reached epidemic proportions. Approximately 39% of adults (>18 years) are overweight (BMI \geq 25 kg/m²) and 13% are obese (BMI \geq 30 kg/m²). An estimated 19% of children and adolescents are overweight and 7% are obese. Prevalence can vary widely among countries.

Throughout the COVID-19 pandemic, obesity has repeatedly been shown to be a risk factor for severe disease progression. However, the role of adipose tissue in viral infection and viral replication of SARS-CoV-2, as well as possible consequences for the metabolism, were largely unclear. This question has now been addressed in a multidisciplinary study.

The research team led by Prof. Dr. Gülşah Gabriel (HPI) and Prof. Dr. Jörg Heeren (UKE) was able to show in autopsy samples of COVID-19 decedents that SARS-CoV-2 is frequently detectable in the adipose tissue of COVID-19 patients. Remarkably, the virus was detected predominantly in the adipose tissue of males who were overweight or obese. In female individuals, SARS-CoV-2 was also detected in adipose tissues, although there was no clear correlation between fat mass and virus mRNA levels. In a preclinical model of the COVID-19 disease, it was also shown that SARS-CoV-2 spreads from the respiratory tract into adipose tissue, where it continues to replicate. This leads to local inflammation and has consequences for the entire metabolism. "*Our results show that the metabolic changes described in patients with COVID-19 can be explained by SARS-CoV-2 infection of adipose tissues,*" explains Jörg Heeren, Professor of Immunometabolism at the Institute of Biochemistry and Molecular Cell Biology at the UKE.

In addition, it was shown that in mature adipocytes (fat cells) in cell culture, intracellular lipid metabolism is a significant factor for the spread of SARS-CoV-2. Thus, blocking lipid degradation by a lipase inhibitor reduces virus replication in mature adipocytes by a factor of 100. Simultaneous administration of a drug used to lower cholesterol further suppressed replication. "*Since these are two agents already approved against other diseases, our results could provide a basis for new treatment strategies against COVID-19,*" Gülşah Gabriel, head of the HPI research department "Viral Zoonoses - One Health" and professor of Virology at the University of Veterinary Medicine Hannover (TiHo) Foundation, explains the results.

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This multidisciplinary study was conducted in the research department of Viral Zoonoses - One Health at the Leibniz Institute for Experimental Virology (HPI), the Institutes of Biochemistry and Molecular Cell Biology, of Forensic Medicine, of Clinical Chemistry and Laboratory Medicine, of Neuropathology, and the Clinics of General, Visceral and Thoracic Surgery and of Intensive Care Medicine at the University Medical Center Hamburg-Eppendorf. The department of Computational Biology of Infection Research at the Helmholtz Centre for Infection Research in Braunschweig was also involved.

Martin Zickler, Stephanie Stanelle-Bertram, Sandra Ehret, Fabian Heinrich, Philine Lange, Berfin Schaumburg, Nancy Mounogou Kouassi, Sebastian Beck, Michelle Y. Jäckstein, Oliver Mann, Susanne Krasemann, Maria Schröder, Dominik Jarczyk, Axel Nierhaus, Stefan Kluge, Manuela Peschka, Hartmut Schlüter, Thomas Renné, Klaus Püschel, Andreas Klötgen, Ludger Scheja, Benjamin Ondruschka, Jörg Heeren and Gülşah Gabriel (2021). **Replication of SARS-CoV-2 in adipose tissue determines organ and systemic lipid metabolism in hamsters and humans.** Cell Metabolism (2021).
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LEIBNIZ INSTITUTE FOR EXPERIMENTAL VIROLOGY (HPI)

The Leibniz Institute for Experimental Virology (HPI) conducts research into human pathogenic viruses with the aim of understanding virus-related diseases and developing new therapeutic approaches. On the basis of basic experimental research, new starting points for improved procedures for the treatment of viral diseases such as AIDS, influenza and hepatitis, but also of emerging viral infections, are to be developed. With its main research areas, HPI covers the world's most important viral infectious agents.

Founded in 1948, the institute's origins go back to the patron Philipp F. Reemtsma and the neurologist Heinrich Pette. As a foundation under civil law, HPI is a non-profit and independent research institution that has been a member of the Leibniz Association (WGL) since 1995. The institute is funded proportionally by the German Federal Ministry of Health (BMG) and the joint research funding of the federal states, represented by the Ministry of Science, Research, Equality and Districts (BWFGB) of the Free and Hanseatic City of Hamburg. In addition, a large proportion is obtained through competitive procedures.

HPI is member of the German Center for Infection Research (DZIF).

More information: www.hpi-hamburg.de

The University Medical Center Hamburg-Eppendorf (UKE)

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