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longCOVID
Decision support for prediction and management of LCS

First Long COVID project's scientific publications

The Long COVID consortium is pleased to inform you that its first scientific papers have already been published.

The 4-year project coordinated by the Helsinki University Hospital aims to understand the mechanisms of host-virus response behind the long-term symptoms following SARS-CoV-2 infection. To do so, Long COVID is studying the pathogenesis of Long COVID Syndrome (LCS) (1) by conducting geographically diverse cohort and registry studies, (2) by conducting mechanistic studies, (3) by using novel high-throughput methods for biomarker analysis, and (4) by conducting interventional and follow-up studies on LCS patients.

SARS-CoV-2 Infection of Human Neurons Is TMPRSS2 Independent, Requires Endosomal Cell Entry, and Can Be Blocked by Inhibitors of Host Phosphoinositol-5 Kinase

To understand the mechanisms of virus infection in the brain, a study led by Dr. Giuseppe Balistreri (University of Helsinki, official Long COVID partner) has been carried out in the frame of the project. Using robotized technologies and state-of-the-art imaging approaches, Dr. Balistreri and his colleagues have discovered the main mechanism of SARS-CoV-2 neuronal infection. The study found that even if brain cells express very low levels of the viral receptor, a cellular protein called ACE2 that is very abundant in the respiratory tissues, SARS-CoV-2 can infect and multiply its genome in human neurons.

The results of this study, published in the Journal of Virology, yet show that the virus first binds to the ACE2 receptor on the surface of neurons, and after being 'swallowed' by the cell, the viral particles are transported into digestive organelles called endosomes and lysosomes. Similarly to our stomach, the endo-lysosomes are full of digestive enzymes. It is thanks to the action of these enzymes that the virus is able to escape from the lysosomes and enter the cell environment where the multiplication and assembly of new progeny virions occurs. By inhibiting pharmacologically, the transport of viral particles from the surface of the cell into the digestive lysosomes, the work demonstrates that it is possible to efficiently prevent neuronal infection.

The group led by Dr. Balistreri is currently investigating whether and how SARS-CoV-2 can spread from one neuron to the next, what are the consequences of viral infection in neurons and non-neuronal brain cells, and formulating more potent and safer antiviral strategies to prevent brain infection.

SARS-CoV-2 infection and viral fusogens cause neuronal and glial fusion that compromises neuronal activity

A collaborative effort between the research group of Dr. Balistreri at the University of Helsinki and the University of Queensland (Australia) let to an unexpected discovery: infected neurons can fuse with the neighbouring cells, a process known as syncytia formation and already observed in the lung cells

but never in neurons. Based on this result, a new paper has been published in the Science Advances journal. The study showed that neuronal function after cell-to-cell fusion is compromised. If this phenomenon occurs in humans, where brain infection by SARS-CoV-2 has already been documented, the main neurological symptoms of Long COVID could be explained.

The Stereotypic Response of the Pulmonary Vasculature to Respiratory Viral Infections: Findings in Mouse Models of SARS-CoV-2, Influenza A and Gammaherpesvirus Infections

In the frame of the project, a study led by Prof. Anja Kipar (University of Zurich, official partner in the project), carried out in collaboration with the University of Helsinki (also a Long COVID partner) and the University of Liverpool, investigated in a comparative way the vascular response in the lungs of mice infected with SARS-CoV-2 and other respiratory viruses (influenza A and murine gammaherpesvirus).

The study, recently published by Viruses, showed that these respiratory virus infections of mice initiate a stereotypic pulmonary vascular response, mediated by arteries and veins, without endothelial infection. This stereotypic reaction is characterised by the recruitment of monocytes and T and B cells, their emigration with accumulation in the vascular wall and their perivascular location. The group is currently investigating the vascular response in the brain of mice infected with SARS-CoV-2, in order to gain further in-depth knowledge on the viral effect on the brain.

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