

Blocking cellular communication stops SARS-CoV-2

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In the transmission of signals within the cell which, for example, stimulate cell growth or trigger metabolic processes, phosphate groups play an important biochemical role. The phosphate groups are often



attached to proteins or removed to control activity. In this process, a change in the protein triggers the next one and the signal is transmitted in a signaling cascade. The target is usually the cell nucleus, where genes are switched on or off.

For the first time, biochemists and virologists from Goethe University have now succeeded in documenting the full picture of all the <u>communication pathways</u> in a human cell infected with SARS-CoV-2 and observed what changes the infection triggers. To do so, they analyzed all proteins carrying a phosphate group at a given moment in time—what is known as the phosphoproteome. The result: SARS-CoV-2 evidently uses above all those signaling pathways of the host cell where a growth signal is transmitted into the cell from outside. If these signaling pathways are interrupted, the virus is no longer able to replicate.

Dr. Christian Münch from the Institute of Biochemistry II at Goethe University explains: "The signaling pathways of the growth factors can be blocked precisely at the point where the signal from outside the cell docks onto a signal receiver—a growth factor receptor. There are, however, a number of very effective cancer drugs that interrupt growth factor signaling pathways slightly further down the cascade, through which the signals of different growth factor receptors are blocked. We've tested five of these substances on our <u>cells</u>, and all five led to a complete stop of SARS-CoV-2 replication."

Professor Jindrich Cinatl from the Institute of Medical Virology at University Hospital Frankfurt says: "We conducted our experiments on cultivated cells in the laboratory. This means that the results cannot be transferred to humans without further tests. However, from trials with other infectious viruses we know that viruses often alter signaling pathways in their human host cells and that this is important for virus replication. At the same time, already approved drugs have a gigantic lead in terms of development so that it would be possible—on the basis



of our results and just a few more experiments—to start clinical studies very quickly."

Via INNOVECTIS, the researchers have patented their method of interrupting signaling pathways by means of specific inhibitors in order to treat COVID-19. INNOVECTIS was founded in 2000 as a subsidiary of Goethe University and has operated successfully since then as a service provider in the transfer of academic know-how into business practice.

More information: Kevin Klann et al. Growth factor receptor signaling inhibition prevents SARS-CoV-2 replication, *Molecular Cell* (2020). DOI: 10.1016/j.molcel.2020.08.006

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