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Researchers at IBEC help identifying a drug in clinical phase that blocks the effects of SARS-Co-V2

April 2, 2020 Research news

IBEC researchers led by ICREA Research Professor Núria Montserrat, together with international collaborators, have identified a drug capable of blocking the effects of the SARS-Co-V2 virus, the origin of the Coronavirus 2019 disease.

The treatment, which can be tested on two hundred Covid-19 patients as of today, has proven effective in mini-kidneys generated from human stem cells. Using hese organoids generated by bioengineering techniques, it has been deciphered how SARS-Co-V2 interacts and infects human kidney cells.

To carry out the study, published today in the prestigious journal *Cell,* the experts have used mini-kidneys created from human stem cells generated at IBEC by Nuria Montserrat's team. These organoids, which

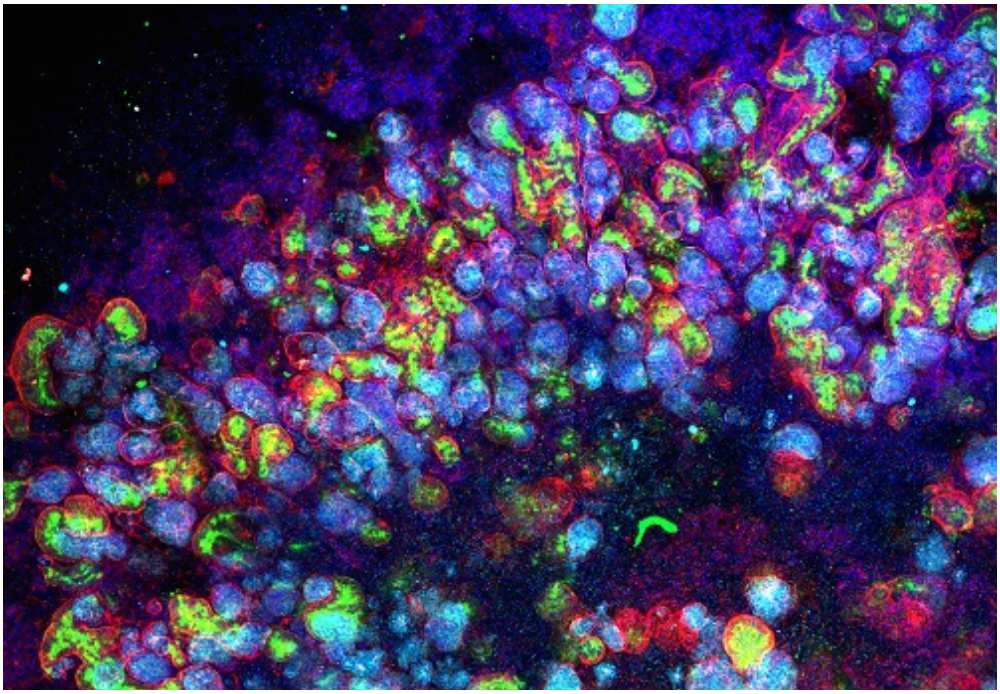
"The use of human organoids allows us to test in a very agile way the treatments that are already being used for other diseases or that are close to being validated. When time is short, these 3D structures dramatically reduce the time we would spend trying a new drug on humans" states Núria Montserrat.

The role of the ACE2 receptor in SARS-Co-V2 infection

Recent publications have shown that to infect a cell, coronaviruses use a protein, called S, that binds to a receptor on human cells called ACE2 (angiotensin-converting enzyme 2). Considering that this binding has been identified as a gateway for the virus to enter the body, avoiding it could constitute a possible therapeutic target.

Following this strategy, the researchers explain that they have focused on understanding the role of the receptor 'ACE2 in these human organoids because they mimic, in a few millimeters almost all the characteristics of a real organ. The study provides new insights on key aspects of SARS-Co-V2 and its interactions at a cellular level, and also how the virus can infect the blood vessels and kidneys.

In addition to the lung, the ACE2 receptor is expressed in multiple tissues, including the heart, blood vessels, intestine, and kidneys, which would explain the multi-organ dysfunction seen in patients. The fact that this receptor is strongly expressed in the kidneys and that SARS-Co-V2 can be found in urine, is what has led the researchers to use these human kidney organoids as a testing model, whose creation Montserrat is an international benchmark.



Confocal image of a kidney organoid that has been generated in vitro by hPSC differentiation in 3D culture using specific renal inductive signals, a methodology that lasts 20 days. Proximal tubule-like structures are detected by LTL staining (in green) and the expression of Laminin (in red) is found in the basement membrane of the renal structures (i.e. Delineatingtubule-likestructures). Nuclei are detected by DAPI staining (in blue). A detail of renal structures within the kidney organoid is depicted at higher magnification on the left, that shows the presence of prominent tubule-like structures (in green) that are delineated by a basement membrane containing laminin (in red).

Identifying an infection-inhibiting drug

First, the researchers proved that the kidney organoids contained different groups of cells that expressed ACE2 in a similar way to that seen in the native tissue, and then proceeded to infect it with SARS-CoV-2. Once they obtained these infected mini-kidneys, they applied different therapies, and, as a result of the study, they concluded that hrsACE2 (human recombinant soluble ACE2), a drug that has already passed phase 1 clinical trials (in healthy volunteers) and phase 2 (in patients with acute respiratory distress syndrome), it significantly inhibits SARS-CoV-2 infections and reduces their viral load.

"These findings identify a promising treatment capable of stopping the infection of the new coronavirus in early stages, which, as of March 30, has affected more than 750,000 people and more than 36,000 lives have been lost due to Covid-

efficacy of experimental treatments and reduce animal experimentation. Now these tools are made available to society once again to try to find solutions to the coronavirus crisis.

Núria Montserrat leads the Pluripotency for organ regeneration group at IBEC and is a member of the Center for Network Biomedical Research in Bioengineering, Biomaterials and Nanomedicine (CIBER BBN). Apart from Núria, Elena Garreta, Patricia Prado and Carmen Hurtado, from her research group at IBEC, have also contributed to this work.

Reference article: Monteil et al, Inhibition of SARS-CoV-2 infections in engineered human tissues using clinical-grade soluble human ACE2, *Cell* 2020, DOI: 10.1016/j.cell.2020.04.004

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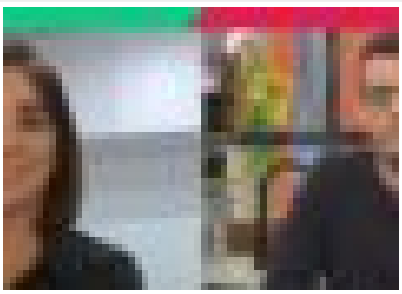

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