COVID 19: Camostat and The Role of Serine Protease Entry Inhibitor TMPRSS2

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Keywords
Angiotensin Converting Enzyme; Human Respiratory Epithelial Cells; Trypsin.

Introduction
According to the latest research, the novel coronavirus uses the protein angiotensin converting enzyme 2 (ACE-2) as receptor for docking to the host cell. Essential for entry is the priming of the spike (S) protein of the virus by host cell proteases. A broadly based team led by infection biologists from the German Primate Centre and with the participation of the Charité Hospital in Berlin, the Hanover Veterinary University Foundation, the BG-Unfallklinik Murnau, the LMU Munich, the Robert Koch Institute and the German Centre for Infection Research wanted to find out how SARS-CoV-2 enters host cells and how this process can be blocked [1]. They have published their findings in the journal "Cell" [1]. The team of scientists was initially able to confirm that SARS-CoV-2 docks to the host cell via the ACE-2 receptor. They also identified Trans membrane serine protease 2 (TMPRSS2) as the cellular protein responsible for entry into the cell [1-3].

Drug description
Camostat (mesylate) is supplied as a crystalline solid. A stock solution can be prepared by dissolving the camostat (mesylate) in the solvent of choice, which should be purged with an inert gas. The camostat (mesylate) is soluble in organic solvents such as DMSO and dimethylformamide. The solubility of camostat (mesylate) in these solvents is about 25 mg/ml. Camostat is a protease inhibitor [1,2]. It inhibits trypsin (Ki=1nM) and various inflammatory proteases, including plasmin, kallikrein and thrombin. Camostat inhibits the incorporation of the severe acute respiratory syndrome coronavirus (SARS-CoV) and the surface glycoprotein SARS-CoV-2 into pseudotyped particles of vesicular stomatitis virus.
(VSV) in vero cells, Calu-3 cells and primary human lung epithelial cells when administered at a concentration of 10 μM [3]. It reduces the number of genomic equivalents of SARS-CoV-2, a marker of infection, in Calu-3 cells. Camostat inhibits the function of the sodium channel in human respiratory epithelial cells (IC50=50 nM) and improves mucociliary clearance in sheep [1]. Administration of camostat (1 mg/kg) inhibits the production of TNF-α and monocyte chemo attractant protein-1 by monocytes and the proliferation of pancreatic star cells in a rat model of pancreatic fibrosis [2].

**Conclusion**

Camostat is in Japan well known as Foipan. SARS-CoV2 uses the cellular transmembrane protease serine 2(TMPRSS2) for docking to the angiotensin-2 receptor. In Japan, Camostat is certified for patients with chronic pancreatitis. In SARS-CoV-2 the first clinical trials were initiated at the University of Aarhus, Denmark. Camostat has the potential to block the entry of the virus into the lung cells, well known as Pneumocytes type 2. To date, no clinical studies were performed, nor are any results present. What we know, Camostat could have a promising potential in COVID-19. Moreover, Camostat given as an inhalative agent like an aerosol could be treatment option the bring the drug to the point where it is needed, in the lungs.

**References**

