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LETTER

The pulmonary-proteoliposome as a new therapeutic approach for Coronaviruses

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ABSTRACT

We are proposingÂ the use of pulmonary-proteoliposome as a new therapeutic approach for Coronaviruses. The designed strategy represents a potential treatment to reduce the overall viral load in the lungs and to help the immune system to successfully stave off the infection.

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The most recent virus to appear, belonging to the family of coronaviridae, is SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2), which causes the syndrome COVID-19 (Coronavirus Disease-2019). SARS-CoV-2 mainly invades alveolar epithelial cells, resulting in acute respiratory distress syndrome that can lead to the death of infected patients.[1] Unfortunately, there are no effective antiviral drugs, and developing a vaccine would likely require years.

To try to overcome these issues, we are proposing a different strategy aimed to reduce the spread of infections by offering a synthetic cell-surface-like competitor to the infectious virus. The competitor works as a bait for the virus. Viruses, like coronaviruses, infect cells through specific proteins on their viral surfaces and hook to a specific host cell membrane receptor. SARS-CoV-2 infection is triggered by the binding of viral S (spike) protein to the ACE2 receptor, thereby enabling viral RNA to enter cells.[2] In our strategy, viruses will be distracted by using protocells, such as 'pulmonary-proteoliposomes,' as competitors. This is a complex formed by the fusion of ACE2 and liposomes.[3] ACE2-like membrane proteins of pharmaceutical interest, are usually obtained from cell lines and combined to Liposomes, which are in vitro self-assembled small (30 nm to several μm) spherical vesicles created from cholesterol and natural nontoxic phospholipids, thus forming a cell membrane-like bilayer. Liposome vesicles are well known for their potential use as drug carriers that are released to the targeted tissue; many studies have demonstrated their safety use for pulmonary administration of different molecules by inhalation.[4] We propose to create proteoliposomes from phospholipids and glycoproteins highly similar to human pulmonary cell membranes that would be used to bait and inactivate coronaviruses. Optionally, the lumen of such proteoliposomes can be filled by a specific drug-like RNase.[5] Such proteoliposomes have limited endocytosis capability and, when taken up into the cell by endocytosis, their contents will follow the endosome-lysosome system for degradation.[6] This would offer an even larger pulmonary-like surface area to infectious viruses that would facilitate virus-liposome interactions and hence virus titration away from the cell, thus preserving the lung tissue from the infection. This approach should, in theory, reduce the overall viral load of the pulmonary tissue while helping the immune system to successfully stave off infection.

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