

Targeted Site-Specific Therapeutics for COVID-19

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ABSTRACT

No definitive therapies for COVID-19 have yet to be identified. The several hundred planned or ongoing clinical trials globally will provide some insights into therapies that may or may not work. The overwhelming majority of therapeutics relies on the systemic delivery of drugs; however, COVID-19 is largely localized to the lungs with some subgroups afflicted in other organ systems. We propose the use of a targeted drug delivery approach in which therapeutics can be delivered using engineered delivery vehicles to reach damaged lung tissue directly.

Keywords: SARS-CoV-2; COVID-19; Targeted drug delivery

PERSPECTIVE

At the time of this letter there are no definitive therapies for COVID-19. The early negative results based on small, underpowered, non-controlled studies and just few open label RCT's are discouraging. Moreover, one study noted that an even higher dose than what was administered may be required to achieve therapeutic efficacy [1]. However, almost all the proposed pharmaceutical therapies for COVID-19 pose at least a few possible adverse effects. Targeted drug delivery of these promising pharmaceuticals might prove to be more effective, enhancing the local effect while attenuating their off-target side effects [2]. SARS-CoV-2 has an affinity for two host cell factors, which are primarily expressed in human lung tissue: ACE-2 and TRMSS2 [3,4]. Considering that COVID-19 primarily affects the lungs in patients with ARDS [5] we propose a targeted drug delivery strategy using different types of drug delivery vehicles such as nano-particle drug carriers, liposomes, viral vectors, perfluorocarbon droplets, and microbubbles. The latter also adheres to sites of damaged vascular endothelium and thus may be a method of systemically

targeting delivery of therapeutics to damaged lungs with SARS-CoV2. For example, perfluorobutane gas microbubbles (PGMC) with a coating of dextrose and albumin efficiently bind to different pharmaceuticals. These 0.3 μm to 10 μm particles bind to sites of vascular injury [5]. Further, the perfluorobutane gas is an effective cell membrane fluidizer. The potential advantages of microbubble carrier delivery include none to minimal (additional) vessel injury through delivery, no resident polymer to degrade leading to eventual inflammation, rapid bolus delivery, and repeated delivery. Microbubble carriers were successfully used in different animal models and clinical trials to deliver antisense oligonucleotide and/or Sirolimus to the injured vascular bed [6-8]. The formulation of microbubbles and therapeutics is easy and can be performed in a hospital pharmacy settings, considering they are currently used widely to enhance diagnostic ultrasound imaging [9]. Given the growing evidence that the most detrimental SARS-CoV-2 reactions are primarily within the respiratory system, localized targeted delivery of therapeutics may prove advantageous over a systemic approach, provided that bioavailability to the target tissue can be proven/verified.

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