CRISPR-based antiviral treatment of coronavirus infections

Unmet Need

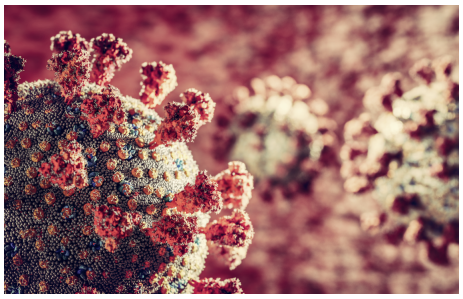
The global market for antiviral drugs is a large one, topping $60B, and is getting larger due to the ongoing COVID-19 pandemic. Spurred on by a $3B investment from the U.S. government into antivirals development, companies such as Pfizer and Merck have developed new treatments for COVID-19 patients. These are important and effective lines of defense against SARS-CoV-2, but it is unclear how well they will work against current and future variants of the virus. Considering the proliferation of SARS-CoV-2 variants as well as the likelihood of future novel coronavirus outbreaks, there is a need for new antiviral strategies against coronaviruses.

Technology

Duke inventors with Ohio State University collaborator Dr. Yizhou Dong have developed an antiviral therapeutic system against coronaviruses. This approach uses a CRISPR-based system which, instead of editing the genome directly, cleaves transcribed RNA – effectively shutting down a gene's expression without lasting genome changes. Specifically, the inventors packaged *CasRx* mRNA and pre-gRNA oligo targeting the *Ctsl* gene, a host protease involved in the entry of coronaviruses into cells, into lipid nanoparticles that selectively target lung tissue. The gene therapy silences expression of the host factor *Ctsl* gene in lung tissue, which blocks the protein from helping the virus enter a cell. This therapy was demonstrated to be effective at inhibiting infection of mouse models by SARS-CoV-2.

Other Applications

This nanotherapy is applicable wherever transient knockdown of gene expression could have a therapeutic



Duke File (IDF) Number

IDF #:T-006715

Meet the Inventors

Wang, Qianben
Cui, Zhifen

Contact For More Info

Ferguson, Christy
919-681-7581
christy.ferguson@duke.edu

Department

Pathology (Dept. & CRU)

Publication(s)

•

External Link(s)

• From the lab of Dr. Qianben Wang
• News story from News-Medical.Net

effect. For example, the inventors have also been able to inhibit expression of previously undruggable genes associated with castration-resistant prostate cancer in cell lines.

Advantages

- Demonstrated effectiveness on multiple variants of SARS-CoV-2, including Delta
- *Ctsl* gene is conserved as an important host factor for viral entry across coronaviruses, providing an attractive target
- Selective delivery to lung tissue
- Highly specific to *Ctsl*, sparing more important but genetically similar cathepsins
- Inhibits SARS-CoV-1 and -2 entry into both TMPRSS2-positive and -negative cells
- Transient effects do not create lasting edits to the genome
- Easily tweaked to target other host or viral factors required for infection by emerging coronaviruses and other threats