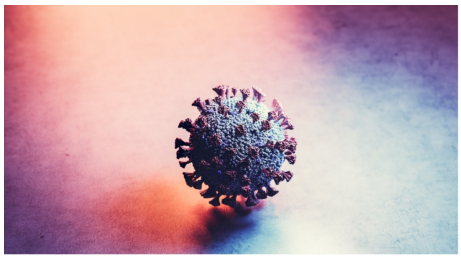
Small molecules that target RNA structures within the CoV genome

Unmet Need

SARS-CoV-2 is the etiological agent of the COVID-19 respiratory disease, the largest scale respiratory virus pandemic the world has witnessed since the 1918 Spanish flu and that has claimed more than 1.4 million lives worldwide. Coronaviruses (CoV family) generally cause mild flu-like symptoms in humans but have caused two smaller scale pandemics in the last two decades: SARS-CoV (2003) and MERS (2012). Recent phylogenetic mapping traced all human coronaviruses to animal origins. While the middle zoonotic carrier of the virus between the animal of origin and humans seem to vary between CoVs, the chronological surfacing of human CoV pandemics seems to follow a dangerous trend of increasing lethality of each pandemic. While recent treatments have been approved for use within hospital settings, there are no known FDA approved cures for the infection. The current limited tools and lack of novel cures underscore the need for a new approach in developing antivirals that would not only provide novel routes to combat the current pandemic but also provide invaluable information on targetable structures that can aid in the prevention of and fight against future CoV outbreaks.

Technology

Duke inventors have reported small molecules intended to serve as lead compounds for CoV RNA-targeted antivirals and chemical probes to further understand CoV RNA biology. Specifically, these are the first small molecules aimed at targeting RNA structures within the 5’-UTR and proximal region of the CoV genome. An amiloride-based small molecule library was screened and select compounds were found that potently inhibited replication competent SARS-CoV-2 as evident



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Meet the Inventors

Hargrove, Amanda
Patwardhan, Neeraj

Contact For More Info

Thomas, Dennis
919-681-7580
dennis.thomas@duke.edu

Department

Chemistry

Publication(s)

External Link(s)

- From the lab of Dr. Amanda Hargrove
- From the lab of Dr. Blanton Tolbert
- From the lab of Dr. Gary Brewer

in the decreased levels of cell free virions in cell culture supernatants of treated cells.

Advantages

- First small molecules aimed at targeting RNA structures within the 5’-UTR and proximal region of the CoV genome
- Foundation for effective CoV antivirals
- Probes for better understanding CoV RNA biology to apply to this pandemic and prepare for those in the future