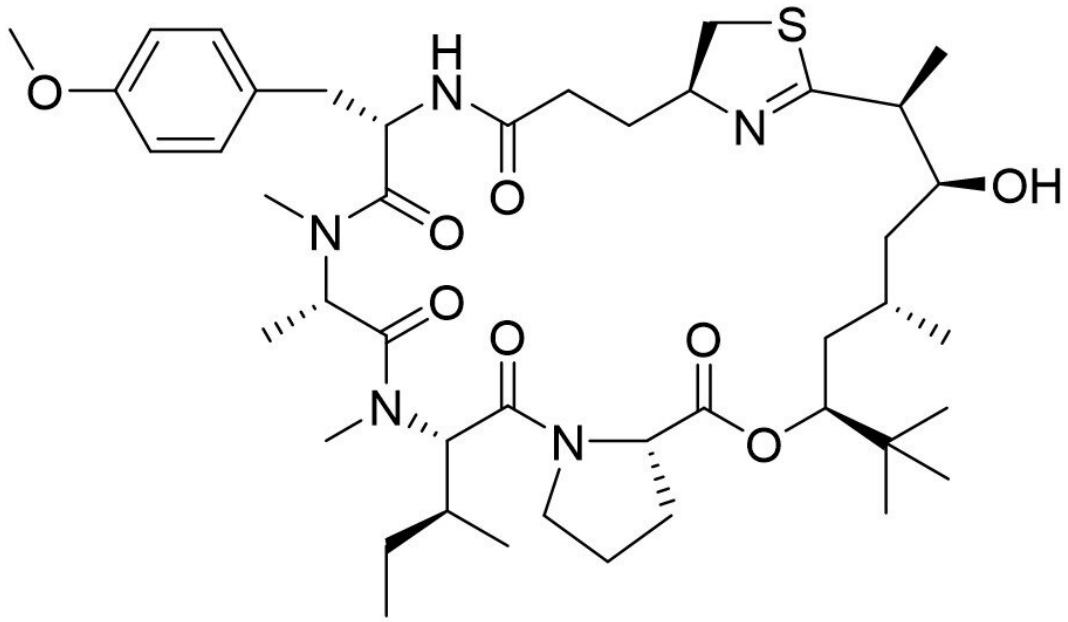
Medical Xpress

Targeting a human protein to squash SARS-CoV-2, other viruses

June 29 2022



Apratoxin S4 (structure shown here) is effective against SARS-CoV-2 in human cells and could be a pan-viral therapeutic. Credit: Adapted from *ACS Infectious Diseases* 2022, DOI: 10.1021/acsinfecdis.2c00008

More than two years into the COVID-19 pandemic, people are realizing that the "new normal" will probably involve learning to co-exist with SARS-CoV-2. Some treatments are available, but with new variants emerging, researchers are looking toward new strategies. In *ACS*

Infectious Diseases, scientists now report that apratoxin S4, an anticancer drug candidate that targets a human protein, can interfere with the replication of many viruses, including SARS-CoV-2 and influenza A, offering a possible pan-viral therapy.

Although COVID-19 vaccines exist, some people who received the shots have still become sick with the disease, and only a fraction of the world's population is vaccinated. That means treatments are still needed, and a few are now available that target the virus's RNA polymerase—the enzyme it uses to make more of its own RNA inside human cells. But some of these drugs, such as remdesivir, don't work unless given at very early stages and can require injections.

In the hunt for new ways to treat COVID-19, various teams have revisited drugs that are already known to fight other diseases, a strategy called "repurposing." One such preclinical stage compound is apratoxin S4 (Apra S4), which is a molecule based on a natural product that has anti-cancer activity. Previous studies have shown that apratoxins can target a human protein called Sec61, which ensures that certain proteins are properly glycosylated and folded correctly. Since viruses don't have their own machinery to do this, they hijack the process and force human cells to make functional viral proteins. Sec61 is essential for the influenza A, HIV and dengue viruses to cause infection, so Hendrik Luesch and colleagues wondered if apratoxins could be a broadly effective, pan-viral medication that could also combat SARS-CoV-2.

In tests with monkey and human cells exposed to SARS-CoV-2, the researchers found that treatment with Apra S4 reduced the number of infected cells compared with remdesivir treatment. The molecule was also effective against influenza A, Zika virus, dengue and West Nile virus infections. Further testing revealed that Apra S4 didn't prevent SARS-CoV-2 from entering cells, but it reduced the amount of viral protein that was produced and transported in cells, especially the spike

protein, and it decreased viral RNA replication. With electron microscopy, the team observed that Apra S4 also largely blocked the formation of new viruses, with many vesicles in SARS-CoV-2-exposed monkey cells having no or very few brand-new viral particles in them. The researchers say more studies are needed, but these results suggest that Apra S4 and other inhibitors of the human Sec61 protein are broadly acting antivirals that could help in the fight against future pandemics.

More information: Sec61 Inhibitor Apratoxin S4 Potently Inhibits SARS-CoV-2 and Exhibits Broad-Spectrum Antiviral Activity, *ACS Infectious Diseases* (2022). DOI: 10.1021/acsinfecdis.2c00008

Provided by American Chemical Society

Citation: Targeting a human protein to squash SARS-CoV-2, other viruses (2022, June 29) retrieved 26 April 2024 from
https://medicalxpress.com/news/2022-06-human-protein-sars-cov-viruses.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.