

Scientific methods identify potential antivirals against chikungunya

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Chikungunya virus has caused two recent massive outbreaks sickening millions of people. Now a team of researchers has shown that several existing compounds have potent activity against the critical CHIKV protease enzyme. The research is published October 10 in *Antimicrobial Agents and Chemotherapy*, published by the American Society for Microbiology.

Chikungunya is a mosquito-borne, largely tropical disease which can cause fever, severe joint pain, headaches, nausea, and fatigue. "Here we exploited an approach that should, at least in theory, be a fast track for the development of compounds useful both for studies of the virus and as leads for development of antivirals," said corresponding author Andres Merits, PhD, Professor of Applied Virology, University of Tartu, Estonia.

"The 3-D-structures of conserved virus proteins are currently second—after the genome sequence—to be resolved for new, medically important viruses," said Merits. Theoretical chemists from among this team used that information to predict in silico what already existing chemicals might bind and inhibit the enzyme.

Then virologists on the team tested the compounds' abilities to inhibit the CHIKV protease' activity in biochemical systems, and then in cultures of infected cells. Several of the compounds proved to be [potent inhibitors](#) of both RNA synthesis and [virus replication](#). Interestingly, it appeared that some compounds used more than one mechanism to

inhibit CHIKV replication. "While none of these compounds is ready to be used as an antiviral drug, they represent promising leads and excellent tools for follow-up studies," said Merits.

The researchers were also able to use their initial findings on which compounds worked to refine the predictive model, said Merits. After that, the success rate rose to fifty percent of the compounds selected by the model that were active against the virus.

"With new viruses constantly emerging, fast and reliable approaches are needed to enable identification of compounds capable of inhibiting their replication," said Merits, alluding to Zika, MERS, and other viruses that were virtually unknown as late as a decade ago. The scientifically selected [compounds](#) are good leads for drug development, and reduce the possibility of subsequent failure. "They are equally important as tools to study and understand the details of [virus infection](#)."

Provided by American Society for Microbiology

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