# New method captures early viral-host protein interactions

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More than 70% of all viruses known to cause human disease, including the one that causes COVID-19, are RNA viruses. They invade the body by hijacking the internal machinery of cells. Yet little is known about how viral RNA commandeers host proteins to replicate the virus.

Now researchers at Vanderbilt University School of Medicine have developed a method to identify the primary interactions between

incoming viral RNA genomes and host proteins. These events are crucial to both viral infection and cellular innate immunity, the host's first line of defense.

The method, called VIR-CLASP (VIRal Cross-Linking And Solid-phase Purification), makes it easier to study potentially all RNA viruses, regardless of their RNA sequence, the researchers reported in the current issue of the journal *Molecular Cell*.

"The number of viral-host interactions at this early stage of infection were thought to be relatively few," said Manuel Ascano, Ph.D., the paper's corresponding author and assistant professor of Biochemistry and of Pathology, Microbiology and Immunology.

"What we have uncovered is a rich tapestry of interactions indicating that the process is far more complex," Ascano said. "This is an unanticipated discovery and, more importantly, suggests that there are novel molecular targets during viral replication that can be disrupted to our benefit."

First authors of the paper are postdoctoral fellow Byungil Kim, Ph.D., and graduate student Sarah Arcos. Graduate students Katherine Rothamel and Jeffrey Jian also contributed to the work.

The researchers first infected host cells with RNA viruses that had been labeled with a unique analog, or form of RNA.

Then they irradiated the cells with a specific wavelength of light to cause the instant formation of crosslinks between the analog-labeled viral genome and proteins from the host cell that interacted with the genome.

This allowed them to capture very early events of infection, at times that previously were inaccessible to scientific investigation.

The cross-linked RNA-binding proteins were then purified and identified using proteomic techniques. Using VIR-CLASP followed by mass spectrometry, the researchers were able to identify hundreds of proteins that directly bind Chikungunya or Influenza A viruses.

**More information:** Byungil Kim et al. Discovery of Widespread Host Protein Interactions with the Pre-replicated Genome of CHIKV Using VIR-CLASP, *Molecular Cell* (2020). DOI: 10.1016/j.molcel.2020.04.013

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