Researchers discover how Zika virus remodels its host cell to boost viral production

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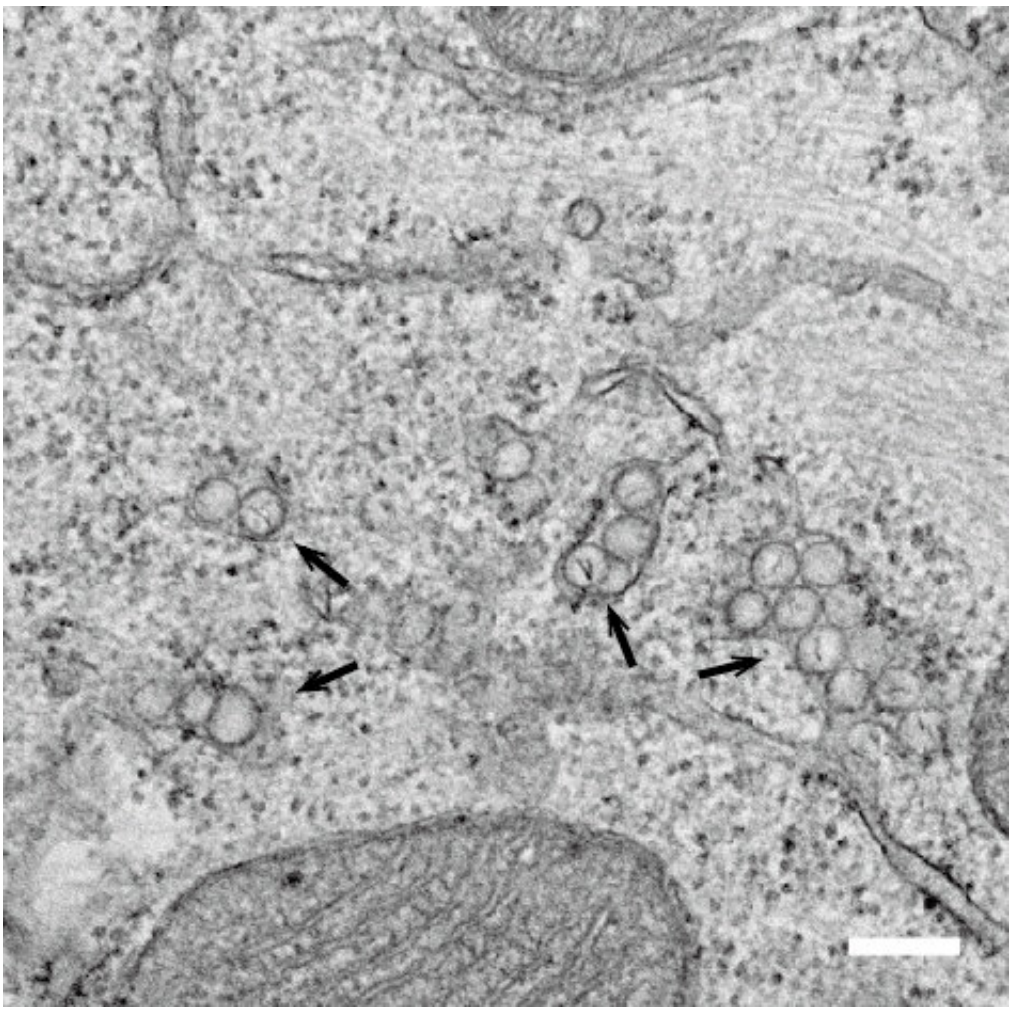


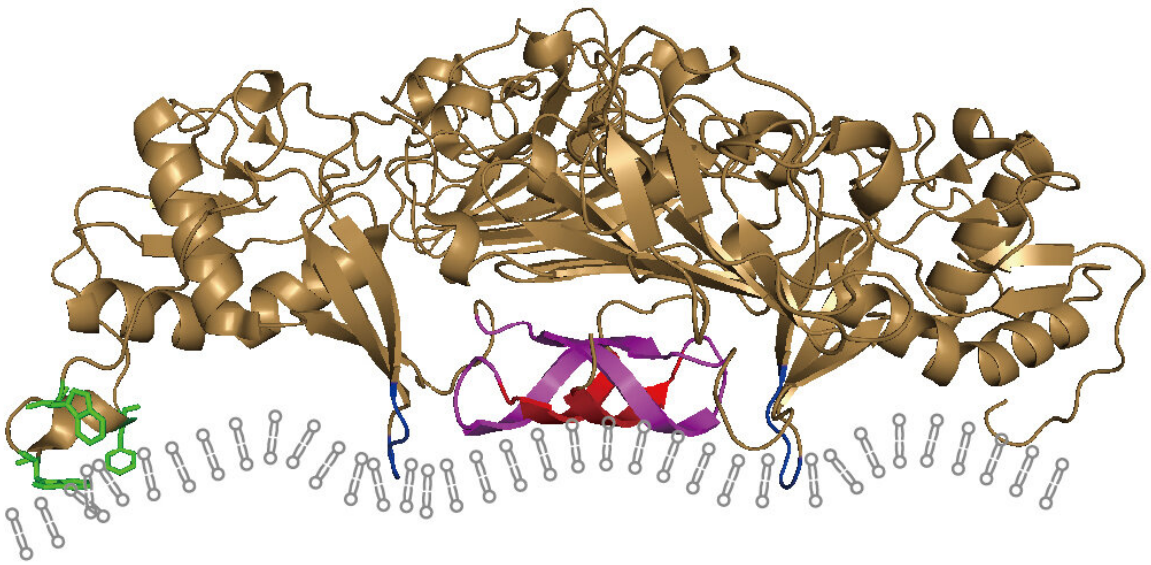
The Zika virus remodels its host cell's endoplasmic reticulum into small pockets (black arrows) where the virus can safely replicate. Ci et al. reveal that this remodeling step is driven by a viral protein called NS1. Credit: Ci et al., 2019

Researchers in China have discovered how a Zika virus protein reshapes its host cell to aid viral replication. The study, which will be published December 23 in the *Journal of Cell Biology*, reveals that the viral protein NS1 converts an interior cellular compartment called the endoplasmic reticulum (ER) into a protective region where the virus can survive and replicate. Blocking this process could be a novel therapeutic strategy to treat patients infected with Zika or similar viral pathogens, such as the yellow fever and dengue viruses.

The Zika virus causes relatively mild symptoms in most cases but can result in severe birth defects when pregnant women are infected. Once the virus enters a host cell, it reshapes the cell's ER, causing this membrane-bound compartment to fold inward and form small pockets where the virus can replicate its genetic material, without being attacked by the host cell's immune defenses.

"The architecture of this viral replication compartment is well known, but how the Zika virus remodels the ER is obscure," says Lei Shi, a researcher at the Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences and School of Basic Medicine, at Peking Union Medical College in Beijing.

In the new study, Shi and colleagues find that this remodeling process is carried out by a viral protein called NS1 that accumulates in the ER of infected cells. The researchers discovered that NS1 inserts itself into the ER membrane, causing it to fold inward and form viral replication compartments. When the researchers mutated NS1 to prevent it from inserting into the ER membrane, the protein was unable to remodel the ER and viral replication was inhibited.



A model of how the Zika virus NS1 protein inserts itself into the ER membranes of its host cell, reshaping them to form a protected viral replication compartment. Credit: Ci et al., 2019

"We conclude that NS1-induced ER remodeling is the basis of replication compartment biogenesis and that viral replication and production are abolished in the absence of this process," says Shi, who co-led the study with Wei Yang, from the Institute of Pathogen Biology in Beijing, and Cheng-Feng Qin, from the Beijing Institute of Microbiology and Epidemiology.

The Zika virus is closely related to a number of other viruses, including the yellow fever virus, dengue virus, and West Nile virus, that also convert the ER of their host cells into specialized viral replication compartments. Shi and colleagues found that the dengue virus's NS1 protein also induces ER remodeling, suggesting that all of these pathogenic viruses use similar mechanisms to generate their replication

compartments and that blocking this process could be a new therapeutic strategy to treat Zika and other viral infections.

More information: Ci et al., 2019. *Journal of Cell Biology* (2019). DOI: 10.1083/jcb.201903062

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