Scientists ID human protein essential for human cytomegalovirus replication

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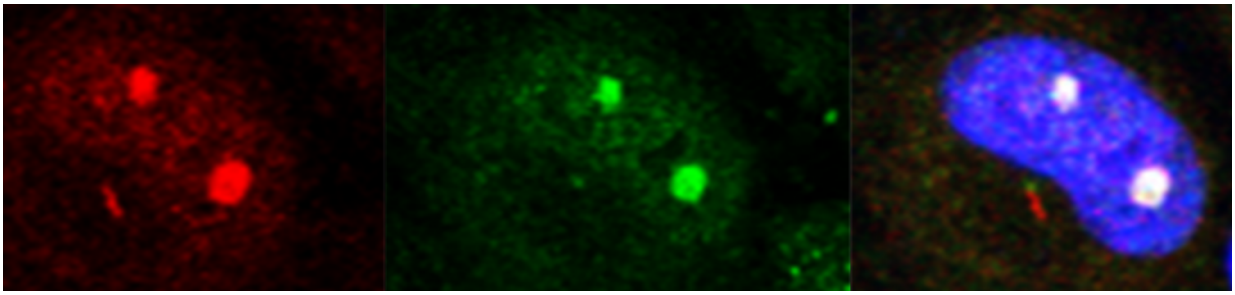

A costaining of VCP and IE2 showing localization of VCP to the viral replication compartments in the nucleus. Credit: Lin Y-T, et al. (2017)

Scientists have demonstrated that a human protein known as valosin containing protein (VCP) is essential for replication of human cytomegalovirus (HCMV). The findings, published in *PLOS Pathogens*, identify VCP as a potential new treatment target.

HCMV infects 30 to 100 percent of people worldwide, depending on socioeconomic status. While most remain symptom-free, HCMV can be dangerous or deadly for people with weakened immune systems or for babies infected before birth. Some HCMV treatments exist, but their benefits are limited, and scientists are investigating new ways to treat and prevent infection.

To better understand how HCMV replicates during active infection, Yao-Tang Lin and colleagues at the University of Edinburgh, U.K., performed a search for human genes needed by the virus for replication. They found that reducing the expression of the VCP gene in HCMV-infected human cells significantly reduced viral replication in the cells.

Additional experiments showed that, without VCP, HCMV is unable to express a critical gene known as IE2. This viral gene is known to be essential for replication and is thought to play a major role when the virus switches from symptom-free, dormant infection to active infection.

Given the critical importance of VCP for HCMV replication, the scientists tested the effects of a chemical known to inhibit the activity of VCP. They found that the inhibitor, known as NMS-873, reduced HCMV replication and IE2 expression in infected cells. NMS-873 appeared to be ten times more potent than Ganciclovir, the most commonly used antiviral treatment for HCMV.

Further research is needed to determine whether NMS-873—originally developed as a potential anti-cancer drug—is safe and effective in humans. Nonetheless, these findings suggest that NMS-873 and other molecules designed to inhibit VCP could potentially serve as HCMV treatments, particularly in patients infected with HCMV strains that are resistant to existing drugs.

"Human Cytomegalovirus infection is an important human disease," the authors further explain. "By gaining a better understanding of how the virus works, we can develop improved antiviral drugs. While more work is required, this study shows the potential of such approaches."

More information: Yao-Tang Lin et al, The host ubiquitin-dependent segregase VCP/p97 is required for the onset of human cytomegalovirus replication, *PLOS Pathogens* (2017). DOI: 10.1371/journal.ppat.1006329