

Press release

Heinrich-Pette-Institut – Leibniz-Institut für Experimentelle Virologie

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Research results
Biology, Medicine
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Human Cytomegalovirus: Phase-separated compartments support replication

Results published in Cell Reports

Hamburg. Human cytomegalovirus (HCMV) replicates its DNA genome in specialized replication compartments, whose exact formation was thus far unclear. A research team from the Leibniz Institute for Experimental Virology (HPI) and the Centre for Structural Systems Biology (CSSB) has now shown that the formation of phase-separated compartments around viral genomes is necessary to recruit the viral DNA polymerase. To form these phase-separated compartments, HCMV uses its UL112-113 proteins. The results have been published in the renowned journal Cell Reports.

HCMV is a leading cause of illness and mortality in immunocompromised transplant patients and the most common cause of congenital infections worldwide.

Upon HCMV infection, the virus replicates its DNA genome in specialized replication compartments in the nucleus of the host cell. These membrane-less organelles emerge as round structures and increase in size over time. However, the exact mechanism of replication compartment biogenesis remains unknown.

In the study now published in Cell Reports, the research team led by Prof. Wolfram Brune (HPI) and Prof. Jens B. Bosse (MHH, CSSB, HPI) used live-cell imaging and photo-oligomerization methods to show that the HCMV proteins UL112-113 undergo liquid-liquid phase separation, which supports the formation of replication compartments in the nucleus. These phase-separated pre-replication compartments are necessary to recruit viral DNA polymerase for viral genome replication.

"Our results show that phase separation is crucial for the formation of pre-replication compartments and viral DNA replication. In this context, the UL112-113 proteins perform an essential function by creating a replication-promoting environment around viral genomes," explains Prof. Wolfram Brune, head of the HPI research department Virus-Host-Interaction.

"Phase separation by the UL112-113 proteins is not only important for the spatial organization of HCMV pre-replication compartments, but also essential for the recruitment of proteins for viral DNA replication," Prof. Jens B. Bosse, head of the HPI-associated Quantitative Virology group, comments on the results.

This study was conducted in the research department of Virus-Host-Interaction at the Leibniz Institute for Experimental Virology (HPI), the Quantitative Virology group (Hannover Medical School, CSSB, HPI), and the Structural Cell Biology of Viruses research department (HPI, CSSB, University of Hamburg). The project was funded by the HPI Strategic Incentive Program (SIP) and is part of the Leibniz ScienceCampus InterACT.

Enrico Caragliano, Stefano Bonazza, Giada Frascaroli, Jiajia Tang, Timothy K. Soh, Kay Grünewald, Jens B. Bosse, Wolfram Brune. Human cytomegalovirus forms phase-separated compartments at viral genomes to facilitate viral

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