Press Release

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LEIBNIZ INSTITUTE FOR EXPERIMENTAL VIROLOGY (HPI)

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Human cytomegalovirus forms phase-separated compartments at viral genomes to facilitate viral replication.
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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 replication.** Cell Reports (March 8, 2022). https://doi.org/10.1016/j.celrep.2022.110469

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LEIBNIZ INSTITUTE FOR EXPERIMENTAL VIROLOGY (HPI)

The Leibniz Institute for Experimental Virology (HPI) conducts research into human pathogenic viruses with the aim of understanding virus-related diseases and developing new therapeutic approaches.
On the basis of basic experimental research, new starting points for improved procedures for the treatment of viral diseases such as AIDS, influenza and hepatitis, but also of emerging viral infections, are to be developed. With its main research areas, HPI covers the world's most important viral infectious agents.

Founded in 1948, the institute's origins go back to the patron Philipp F. Reemtsma and the neurologist Heinrich Pette. As a foundation under civil law, HPI is a non-profit and independent research institution that has been a member of the Leibniz Association (WGL) since 1995. The institute is funded proportionally by the German Federal Ministry of Health (BMG) and the joint research funding of the federal states, represented by the Ministry of Science, Research, Equality and Districts (BWFGB) of the Free and Hanseatic City of Hamburg. In addition, a large proportion is obtained through competitive procedures.

HPI is member of the German Center for Infection Research (DZIF).

More information: www.hpi-hamburg.de